A CLINICO – HISTOPATHOLOGICAL STUDY OF REACTIONS IN LEPROSY

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DERMATOLOGY, VENEREOLOGY AND LEPROSY

(BRANCH XII A)

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DECLARATION

I, **Dr. R. Manoharan**, solemnly declare that dissertation titled,

"**A CLINICO – HISTOPATHOLOGICAL STUDY OF REACTIONS IN LEPROSY**" is a bonafide work done by me at The Department of Dermatology, Govt. Stanley Medical College & Hospital during 2007 – 2010 under the guidance and supervision of **Dr. K. Manoharan M.D D.D., Professor and Head of Department,** and **Dr. R. Madhu M.D(Derm)** Asst. Professor, Department of Dermatology, Govt Stanley Medical College, Chennai – 600 001.

The Dissertation is submitted to **The Tamilnadu Dr. M.G.R. Medical University**, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch XII - A) in Dermatology, Venereology and Leprology.**

Place :

Date:

(Dr. R.Manoharan)

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CERTIFICATE

Certified that this dissertation entitled "**A CLINICO HISTOPATHOLOGICAL STUDY OF REACTIONS IN LEPROSY"** is a bonafide work done by Dr. R.MANOHARAN, Post Graduate Student of the Department of Dermatology, Venerology and Leprosy, Stanely Medical College, Chennai – 600 001. During the academic year 2007-2010. This work not previously formed on the basis for the award of any degree.

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CONTENTS

INTRODUCTION

Leprosy is a chronic granulomatous disease caused by Mycobacterium leprae. It is also known as Hansen's disease since its causative agent was first described by a Norwegian physician, Gerhard Henrik Armauer Hansen in 1873. Mycobacterium leprae has the distinction of being the first pathogenic organism to be discovered. Leprosy as an infection in man could be compared to a peat fire which keeps smouldering for a long time but suddenly bursts into flames when conditions are favourable, such sudden flares in the course of leprosy are referred to as reactional states in leprosy. This thesis is an attempt to study the Type I and Type II lepra reactions in detail with special reference to the clinical features and histopathology.

REVIEW OF LITERATURE

Definition :

In clinical terms the word reaction is used to describe the appearance of symptoms and signs of acute inflammation in lesions of a patient with leprosy.

In immunological terms, reactions are episodes of acute hypersensitivity to bacterial antigens, brought about by a disturbance of the pre existing immunological balance.

Classification :

Various authors Muir.E (1948), Cochrane (1964), Dharmendra (1967), Madrid Congress (1953), Rio Congress (1963), Jopling W.H (1971), Waters M.F.R (1971) propounded various classifications at different times with different terminologies. At present the classification by Jopling W.H is adhered to :

1. Type I lepra reaction - Reversal reaction
   - Downgrading reaction
2. Type II lepra reaction
3. Type III lepra reaction

Synonyms for reactional states in leprosy

1. Leprosy reaction (Jopling W.H)
2. Lepra reaction (Muir.E)
3. Acute phases in leprosy (Cochrane R.G.)
4. Acute exacerbations in leprosy (Dharmendra)
5. Type I reaction (Bryceson)
    a) Borderline reaction

b) Tuberculoid reaction

c) Non lepromatous lepra reaction

6. Reversal reaction – upgrading reaction
7. Type II reaction
   a) ENL reaction
   b) Lepra fever (Ramu and Dharmendra)
   c) Lepromatous lepra reaction (Bryceson)
8. Type II reaction – Lucio Phenomenon

The plethora of terms give rise to confusion and there is a need for unified criteria for better understanding. The universally accepted terminology is that given by Jopling W.H. which can be employed by all to avoid use of confusing terminologies in the future.

HISTORICAL ASPECTS

Type I reaction :

In 1955 Wade H.W[1] first used the term "Reversal reaction" to describe the appearance of skin lesions resembling those of tuberculoid morphology in presumed cases of lepromatous leprosy. Desouza Lima reported a similar reaction as "Pseudo exacerbation" and Tajiri[2] as "acute lepromatous infiltration". The term "upgrading reaction" was first used

by Ridley in 1969, though Tajiri[2] had earlier attempted to distinguish upgrading and downgrading reaction in 1955.

Type II reaction :

Type II reaction was originally introduced as erythema nodosum leprosum. This term appeared in a paper written by Dr. M. Murata as early as 1912[3]. But surprisingly for more than 50 years, ENL was not recognized outside Japan.

In 1939, Desouza Lima and Maurano[4] had written that erythema nodosum was seen as the most frequent cutaneous symptom of lepra reaction, but it differed from classical erythema nodosum in which the lesions seldom affected the face or the nerves.

In 1942, Pecorano[5] made a particular attempt to delineate the differences between erythema nodosum leprosum (ENL) and erythema nodosum of other etiologies and stated that ENL was considered the most frequent acute skin manifestation of lepra reaction and was seen usually in advanced cases, probably signifying improvement in prognosis. Pogge and Ross[6] stated in an article entitled "Erythema nodosum in leprosy" (1946) "Leprosy is a chronic disease in which there are at least at times acute manifestations, the local lesions of which may be those of erythema nodosum or less often erysipeloid reaction of the skin, painful neuritis or painful lymphadenopathy". They pointed out that erythema nodosum seen with leprosy was neither caused by nor cured by sulfone therapy.

Wolcott R.R.[7] was one of the first attempt to differentiate erythema nodosum from other acute reactions. He pointed out that erythema nodosum has become much more common since the initiation of sulfone therapy. He pointed out that there was a correlation between anti leprosy treatment and the appearance of erythema nodosum as indicated by observation that 7% of cases occurred before treatment and 93% afterward. He also suggested that the presence of erythema nodosum indicated an increasing resistance to the disease.

Schujman S[8] believed in a beneficial influence of lepra reaction on the evolution of lepromatous cases and pointed out that however frequent, intense and prolonged the reactions were they were beneficial to the patient. He said that favourable effects were greatest when they appeared in the early stages of the disease. He also said that "Reactions may sometimes cause clinical and bacteriological clearing of the lesions". It was presumed that early occurring reactions are same as those that show bacteriological clearing and that represent the "Reversal reactions", while the reactions clearing later were probably ENL cases.

Roche et al[9] thought that the lepra reactions were essentially useful and that their occurrence in a patient represented a favourable sign..

Contreras et al[10], stated early in 1952 that lepromatous lepra reaction is a grave syndrome with serious changes that might lead to generalized amyloidosis and a fatal outcome.

Davison A.R.[11], pointed out that higher the original bacteriological index, the more likely it was that ENL would develop. He concluded that ENL had a bad prognostic significance.

In 1959, W.H. Jopling[12] introduced the terms Type I and Type II reactions and differentiated them.

Type III reaction (Lucio Phenonemon)

This was first described by Lucio and Alvarado in Mexico in 1852. They described it as a necrotizing skin reaction in diffuse non nodular leprosy. They called this reaction "Lepra manchada". The eponymic designation "Lucio's phenomenon" was proposed by Latapi in 1948. It was Latapi and Zamora[13] who brought the paper to the notice of the medical world.

EPIDEMIOLOGY :

PREVALENCE :

Type I Reaction : These occur in about 30% of patients with immunologically unstable borderline forms of Leprosy[14].

Type II Reaction : ENL occurs among 35% of patients in all age groups and 0 - 3.1% of pediatric patients with lepromatous leprosy[15,16].

INCIDENCE :

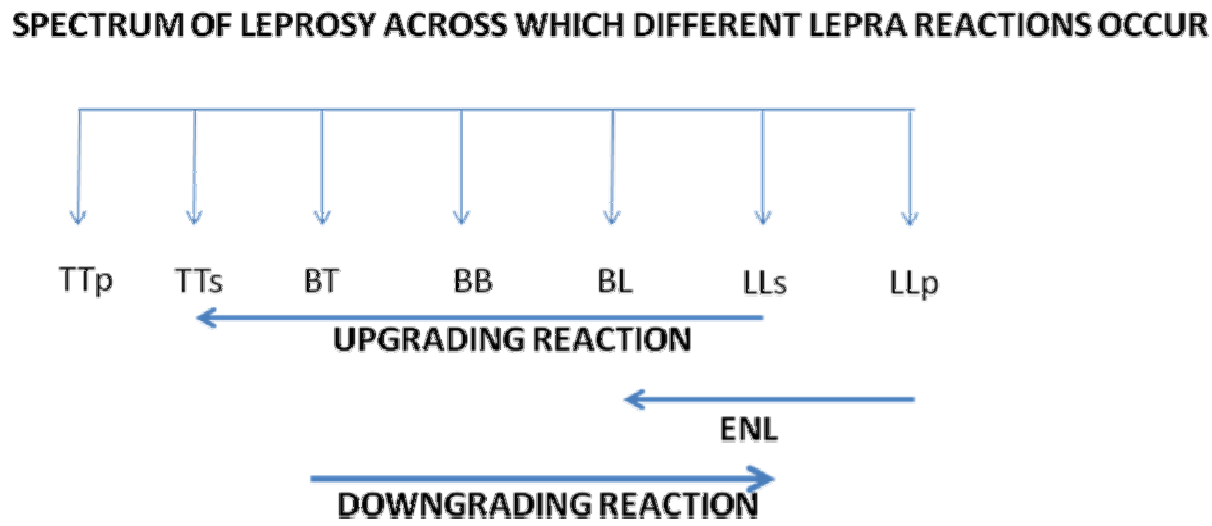
Age:

Both Type I and Type II reactions occur mainly in the age group of 20-40 years. The highest incidence of ENL reaction has been noted between 11-40 years, corresponding to the highest age incidence of leprosy in South India[17]. There is a high prevalence of leprosy in children. Majority of them tend to have indeterminate or tuberculoid type of leprosy[18]. Despite the high prevalence of leprosy in children, the occurrence of both type I and type II reactions especially erythema nodosum leprosum is exceedingly rare.

Sex :

Both Type I and Type II reactions occur in both the sexes with almost equal frequency. Nerve damage is unlikely in women especially in reactions associated with pregnancy. The predominance of males[17] in a study of erythema nodosum leprosum cases in South India[19] had been attributed to the high proportion of male patients attending the hospital (10:1). Browne[20] had reported a higher incidence among males while Guinto[21] found more females. The neuritis of type I reaction is much more common in patients with borderline tuberculoid leprosy.

TYPE OF LEPROSY :



All types of leprosy can manifest some form of reaction except the indeterminate type.

Type I reaction:

It is typically seen in borderline spectrum of leprosy because of their immunological instability (i.e. BT,BB, BL). It also occurs in 10% of patients with subpolar lepromatous leprosy, after treatment[22]. Borderline patients may upgrade to the tuberculoid type(TT) but form a subgroup-secondary tuberculoid or TTs[23], which in contrast to its counterpart at the other end of the spectrum (LLs or subpolar) appears to be immunologically stable[24].

Type II reaction :

It usually occurs in patients with multibacillary disease, who had enough treatment to reduce the morphological index to <5%[25] and rarely de novo in some cases. More than 50% of patients with lepromatous

leprosy (LLp and LLs) and 25% of patients with borderline lepromatous (BL) leprosy suffer from Type II reaction.

Earlier it was believed that histoid leprosy does not go in for erythema nodosum leprosum. But more recently, erythema nodosum leprosum has been reported by some authors, [26,27,28,29] and is now occasionally observed in clinical practice.

Type III reaction : (Lucio phenomenon)

This type of reaction is confined to the diffuse, non nodular form of lepromatous leprosy (Lucio leprosy), which is chiefly encountered in South and Central America. One case has been reported from Iran. Among its unique features is the fact that it is seen only in untreated patients.

ONSET OF REACTION WITH REFERENCE TO INITIATION OF TREATMENT

Both type I and type II reactions are seen in approximately 25% of the untreated patients and 50% of treated patients.

Reversal reaction

More than 50% of the patients with BT and BB spectrum of leprosy develop reaction between 2 weeks and 6 months of starting therapy. About 50% of BL leprosy patients develop type I reaction, usually between 2weeks and 12 months after starting multi drug therapy,

but sometimes later also if they had downgraded to almost lepromatous spectrum[30.] Kumar et al reported that incidence of reversal reaction was highest during 6-12 months after starting multidrug therapy[31].

Type II reaction :

In about 50% of the patients, ENL reaction occurs during the 2nd & 3rd years following treatment[26]. The reaction is seen when the skin lesions appear quiescent and all or most of the bacilli in the skin are granular[24]. In the report by Kumar et al, erythema nodosum leprosum was noted to occur mostly during the 2nd or 3rd year after starting MBMDT[31].

However inspite of the above facts, a patient may present with reaction, either type I or type II when first seen. A publication from Los Angeles reported a series of 32 adults presenting with reaction for the first time and 22 (69%) had ENL[32]. In a study reported from India 40% of patients diagnosed with lepromatous leprosy presented with ENL at the first visit.[29]

PRECIPITATING FACTORS

Lepra reactions are known to be precipitated by definite factors. They include drugs, stress, vaccinations, pregnancy etc. Wolcott (1947) had reported in his study that the incidence of lepra reactions rose more than 7% in the pre sulphone era to 93% in the post sulphone era.

Type I reaction

Upgrading reaction may be precipitated by institution of antileprosy treatment especially dapsone, post partum state, when there is rapid gain of cellular immunity lost during pregnancy, due to lepromin testing and when immunotherapy in the form of sensitized lymphocytes / lymphokines is administered.In patients with BTHD, reversal reactions may occur spontaneously, even before initiating treatment.

Downgrading reaction may be precipitated by psychological stress, intercurrent infections, malnutrition and vaccination including BCG.[25,33]

It may also be precipitated by hyperthyroidism,[34] oral contraceptive pills,[35] pregnancy[25], labour[22] and hormonal factors including puberty[22].

Type II reaction

The factors which are well known to precipitate Type II reaction include psychological stress, physical stress, surgery, physical injuries, menstruation, pregnancy, parturition and puberty. Ingestion of alcohol,[36] potassium iodide, Vitamin – A,[33] hot foods,[36] mantoux testing, vaccinations, extremes of heat / cold,[37] intercurrent infections like malaria, filariasis, chicken pox, typhoid etc and drugs including dapsone[38], longer acting sulphonamides[38], thioacetazone[38],rifampicin[38] etc are also postulated to play a role in precipitating Type II reactions.

Some agents which were used as antileprosy agents in the past and precipitated ENL but are now more of historical interest include

Hydnocarpus oil injection,[39] diphenylthiourea and sulphamethopyrazine. It was previously postulated that Mycobacterium immunotherapy in the form of intradermal injections continued along with MDT can precipitate reactions. However a recent study shows no statistically different incidence of reactions in Mycobacterium w administrated group compared to a control group administrated only MDT[40].

CLINICAL MANIFESTATIONS :

Reactions are responsible for many of the symptoms that occur in leprosy including virtually all the symptoms of the disease that arise acutely. Reactions often compel the patient to seek medical attention for the first time. Remissions and exacerbations are the hallmark of reactions. The signs and symptoms of different types of reactions are as follows:

Type I reaction :

Clinically, the most prominent sign is a rapidly developing change in the appearance of one or all the skin lesions - they become swollen and raised, erythematous, more prominent, shiny, warm to touch, often tender or ever painful resembling erysipelas. It can occur virtually in any site of the body infiltrated by a hypopigmented hypoanaesthetic patch of borderline leprosy. In 2004, a case has been reported by Dogra et al[41] in which phimosis was the presenting complaint of the patient, which finally

turned out to be a borderline lepromatous Hansen's disease in Type I reaction. In another case report by Gupta et al[42], of a 4 year old male child diagnosed with borderline lepromatous leprosy, erythematous infiltrated plaques of Type I reaction have been described in the scrotal skin. Sometimes necrosis supervenes with breakdown and ulceration. The ulceration is usually superficial and heals quickly with anti-inflammatory therapy. The lesions desquamate as they subside and ultimately flatten leaving a wrinkled surface. If the lesion has been prolonged or severe, there may be scarring. Untreated Type I reaction tends to last for months or years and may relapse. The nearer the patient is to the centre of the spectrum, greater the number of lesions that get involved and more severe the changes.

In patients undergoing reversal reaction, new lesions are unusual, but when they appear, they present with well defined tuberculoid characteristics with discrete and thickly infiltrated margins. During the downgrading reaction many new lesions may appear and these will not tend to show the marginal definition of pre existing lesions. After each downgrading reaction, the lesions assume more and more borderline characteristics.

Another manifestation of type I reaction is edema of the involved site. It can occur over hands, feet or face either independently or together. Edema of the prepuce has produced phimosis[41]. Tenderness of the palms

and soles are present occasionally and may sometimes herald an upgrading reaction.

Neuritis is the most important component of a Type I reaction. It may occur together with skin changes or independently. Neuritis presents classically with tender enlargement of nerves at the site of prelidiction. Apart from the nerve being painful, the pain may be referred to the region of the skin which it supplies. Nerve pain causes a great deal of suffering and loss of sleep. There may be associated loss of function due to involvement or compression of the motor fibres with sudden onset of paralysis of the muscles of hand, foot or face resulting in wrist drop, foot drop or facial palsy including lagophthalmos. Anaesthesia develops rapidly in the region of distribution of the affected nerve. Facial palsy is most likely to occur when there is a lesion on the cheek. Involvement of the zygomatic branch is very common resulting in paralysis of orbicularis oculi muscle and only rarely a lower facial paralysis is seen. In facial nerve lesions inside the facial canal there were cases in which the chorda tympani along with only a single branch of facial nerve were involved instead of the full nerve. Sometimes the neuritis remains asymptomatic. Silent neuritis is seen in cases there is only slight or no tenderness on palpation of the nerve, but there is an increase in anaesthesia or weakness of muscles supplied by that nerve. Small cutaneous nerves that lie within a reacting patch may be completely destroyed so that a permanent patch

of anaesthesia remains. This is uncommon on the face since there exists a considerable overlapping of sensory supply of different cutaneous nerves. Rarely, a nerve abscess forms, producing a fluctuant, tender swelling along the course of a nerve especially ulnar nerve, greater auricular nerve etc.

In patients co infected with HIV, who are treated with highly active anti retroviral therapy (HAART), Type I reaction may manifest as a form of immune reconstitution inflammatory syndrome[43]. HIV generally has no significant effect on the clinical course of treated and untreated leprosy. However it has been reported that neuritis in co-infected people can be more severe and the reversal reaction may be more frequent after therapy[43]. It is usually seen in the first few months of starting HAART (within 6 months). It usually results from an increase in cell mediated immunity.

Systemic disturbances are unusual but severe reactions may be accompanied by systemic illness characterized by low grade fever, malaise and anorexia.

Tenosynovitis of extensor tendons over that back of wrist may develop during Type I reaction.

Grading of Type I reaction[110] :

1. Mild – Erythematous raised skin lesions with no evidence of neuritis.

2. Moderate - Erythematous patches/ plaques with effusion of joints
3. Severe – Ulceration of the skin lesions/ neuritis causing paralysis or impending paralysis.

In downgrading reaction from BL → LLs, bacillary invasion of previously unaffected organs especially the mucosa of the upper respiratory tract, eyes, phalanges and testes may occur.-

Type II reaction :

Type II lepra reaction or Erythema nodosum leprosum (ENL) can be classified as follows, based on mode of onset of reaction[45].

1. Rheumatic type – Starts with fever, joint manifestations and skin lesions manifest later.
2. Exanthematous type – Starts with fever and skin lesions simultaneously.
3. Mixed type – Starts with fever, skin lesions and joint manifestations simultaneously.

Grading of Type II reaction[45]

1. Mild – Temperature upto 100° F and a few skin lesions on one or more extremities.
2. Moderate – Temperature upto 102°F. Skin lesions are more numerous in all four limbs and few on the trunk and face with occasional vesicles and pustules. Extracutaneous signs present.

3. Severe – Temperature above 102°F. Vesiculation and pustulation present. Visceral involvement present.

Cutaneous manifestations:

Erythema nodosum leprosum (ENL) is the most outstanding cutaneous manifestation of type II reaction. ENL was described by Green(1929) as "an acute exanthem of leprosy". This presents most commonly as small 2.5mm papules or larger nodules which are warm, painful and tender. They may be superficial and standout clearly from the skin or may be placed deeply and be more palpable than visible. They are dome shaped with ill defined margins and erythematous to dusky brown in colour. They tend to appear in crops, blanch with light finger pressure and are evanescent lasting only 2-3 days, rarely longer. If multiple, they tend to be distributed bilaterally and symmetrically. Fresh crops of erythema nodosum leprosum tend to appear between 5.00 to 6.00PM, a time when endogenous cortisol production is at its lowest. ENL occurs as bilaterally symmetrical lesions anywhere where there has been a lepromatous infiltrate, although this may not have been obvious clinically. ENL lesions are more common on the face, arms, flexor aspects of forearms, and medical aspect of thighs, but the trunk is also a common site. In fact they may appear on any skin area excluding the hairy scalp, axillae groins, perineum and other intertriginous areas as these are warmer regions of the body avoided by M.leprae. These may

occasionally be seen on palms and soles. ENL lesions subside with desquamation and leave behind a bluish stain in the skin. In case they do not resolve completely, a chronic painful panniculitis develops which may persist for months to years. Subsequently larger areas of inflamed skin, and subcutaneous tissue then become fixed to the underlying fascia, muscle or bone and may thus immobilize a hand / foot or even face. [Eg : Reaction of the hand with panniculitis of the dorsum of hand and arthritis involving interphalangeal joints]. This tissue is poorly vascularised any may ulcerate even with minimal trauma. The ulcer then heals slowly over weeks to months.

Apart from the classical ENL, Type II reaction can also manifest as vesicular, bullous, haemorrhagic (esp. around the edges of palms, soles), pustular (sterile pus containing polymorphonuclear leukocytes and degenerated AFB), ulcerated (erythema necroticum ulcerans) and erythema multiforme like lesions[46]. A few cases of bullous ENL have been reported from Mexico, South America, India and one case has been reported from Nepal[47]. In bullous ENL, the histopathology usually shows an intra epidermal cleft with diffuse polymorphonuclear infiltrate and a few foamy histiocytes along with a few AFB[47]. Erythema necroticum ulcerans has been reported occasionally in adults, but not in paediatric patients barring one case report by Pandhi et al[16]. Pustular and hemorrhagic ENL carry poor prognosis[45]. ENL lesions tend to recur at the

same site. Apart from ENL, pretibial ulceration may also be seen in Type II reaction (due to dysproteinemia)[45].

The relationship between leprosy and HIV infection remains obscure due to conflicting reports appearing over a period of time. By analogy with the development of active tuberculosis and other mycobacterial infections among HIV positive patients, an increased prevalence of leprosy was expected, particularly towards the lepromatous spectrum and possibly also the prevalence of ENL in areas where leprosy and HIV are endemic. Earlier literature is replete with reports of increased frequency of Type I reactions (reversal reactions) severe neuritis, poor therapeutic outcome and relapses among HIV infected leprosy patients[48]. HIV coinfection was thought to decrease the risk of ENL until recently when reports of ENL among coinfected patients started to appear. Gebre et al[49] recorded a definite higher risk of ENL reactions. Nand Lal Sharma et al[48] also reports similar findings. HIV is neurotrophic and may cause necrotizing vasculitis of the nerves[50]. Possibly the interaction of neurotropicity of both M.leprae and HIV may result in neuropathy that is severe and unresponsive to steroid therapy[51]. Vreeburg et al[52] also noted that although neuritis is equally common in both HIV positive and HIV negative patients, the therapeutic outcome with steroids was poorer in the HIV positive group.. Similarly HIV induced vasculopathy might aggravate immune complex mediated

vasculitis/ panniculitis of ENL that responds poorly to steroid therapy[48]. The exact pathologic mechanism of ENL among these co infected patients is however, not fully understood. To summarise, increased incidence of ENL has been reported to occur in HIV co infected patients in some studies which is also poorly responsive to steroid therapy. This is an emerging area which needs further evaluation.

Neuritis :

Type II reaction often causes neuritis. In a severe reaction, nerves may become painful and lose function rapidly. But more often the neuritis is less dramatic than in type I reaction. Affected nerves are tender and a little enlarged.

Constitutional symptoms :

Type II reaction often produces a generalized systemic illness which may be severe. The fever which usually begins in the evenings, is usually of high grade, associated with chills and rigors. The patient may become exhausted and prostrated by pain, headache myalgia anorexia, insomnia and depression. The fever falls by lysis. Oedema of the face, hands & feet and painful dactylitis are other general manifestations of Type II reaction.

Ocular manifestations :

The ocular manifestations of ENL include conjunctivitis, keratitis, scleritis, episcleritis, lagophthalmos, iridocyclitis and secondary

glaucoma. Among them iridocyclitis is the most dreaded and is the most common cause of irreversible blindness in leprosy. It manifests as redness, decreased vision, pain of the whole eye which often radiates to the brow and the temple, photophobia, and epiphora. The eyelids are swollen in severe cases secondary ocular inflammation and hyperemia. The eye is diffusely erythematous with the most intense erythema at the limbus 360° around the cornea (ciliary flush) and severe ocular tenderness. There is loss of luster of the cornea due to corneal edema and presence of inflammatory cells and proteins in the aqueous humour (flare and cells). The pupil of the affected eye is usually smaller than that of the other eye. The above symptoms may be present in varying degrees depending on the severity of the reaction. Any delay in initiation of treatment may results in permanent loss of vision.

Till date, involvement of orbit in ENL has been reported only in one patient, where it presented as orbital apex syndrome[54]. While vasculitis due to Wegener's granulamatosis and periarteritis nodasa have been implicated in orbital apex syndrome, only in the one patient, it has been described to be due to ENL. Involvement of the sinuses by lepramatous process is a well recognized entity. In the patient described by Dhaliwal et al[54] , there was involvement of left maxillary and ethmoidal sinus and destruction of medical orbital wall, vasculitis of which probably spread to the orbit. Any inflammatory process involving

the orbital apex (superior orbital fissure) affects III, IV, V and VI cranial nerves, resulting in complete ophthalmoplegia, loss of vision and decreased ocular sensations. Vasculitis may affect the ophthalmic, posterior ciliary or central retinal artery causing abrupt blindness, while inflammation of the connective tissue around the blood vessels can produce proptosis. All these conditions are ocular emergencies and that require urgent expert management.

ENT manifestations :

Erythema nodosum leprosum can involve nasal and buccal mucosa, tongue and palate. It may result in nasal blockade, pain, difficulty in breathing, rhinitis, epistaxis, erosion, ulceration and perforation of the nasal septum. Involvement of the soft palate may result in ulceration and destruction of the uvula, deformity and scarring over the fauces. In the hard palate, erosion, ulceration and perforation[55] can occur as a part of Type II reaction. In the past, involvement of larynx and consequent respiratory embrassment, raucous voice and aphonia have been described[45]. Cough and hoarseness of voice may also occur in ENL due to involvement of larynx. The gums may also be involved resulting in diffuse swelling of the gums.

Musculoskeletal manifestations :

Myositis is a manifestation of type II reaction. The muscles particularly the vasti and brachioradialis may feel woody hard. Further

more, firm, painful and tender nodules can occur in muscles rendering their movements painful. In the bones, periosteitis can affect tibia, phalanges, upper end of ulna, lower end of fibula and calcaneum. In the tibia, it clinically manifests as painful, soft and tender swelling, thickening and increased anterior curvature. Radiologically, the features include periosteal elevation, thickening of the cortex and increased anterior curvature. In the phalanges, the manifestations are pain and spindle shaped swelling (dactylitis). Osteoporosis is another manifestations of Type II reaction. It affects mainly the phalanges, metacarpals, long bones and ribs. Radiologically it manifests as pseudocysts (punched out areas of rarefaction). Resultant pathological fractures and subarticular collapse of bones causing shortening of digits may occur. “Double stripe sign” in bone scan may be seen over distal tibiae[56]. It is also seen in hypertrophic osteoarthropathy.

The joint manifestations of Type II reaction are arthralgia and arthritis with resultant non paralytic deformities. The joint manifestations are reportedly inversely proportional to the skin lesions[45]. The radiological findings include soft tissue swelling, osteoporosis, sub articular collapse, ankylosis and disorganization.

Lymphadenitis :

The lymphnodes are inflamed in 50% of patients with ENL. Preauricular lymphadenitis is a premonitory sign of Type II reaction[45].

Other lymph nodes which may be involved include cervical, axillary, intercostal and inguinal nodes. Initially they are discrete and tender, but later become matted. In very rare instances, there may be necrosis and discharge through the skin[53].

Cardiovascular manifestations :

During Type II reaction the blood pressure is low. The blood vessels show leprous vasculitis and leprous meningovasculitis[45]. Pericardial friction rub has been reported.

Respiratory system manifestation :

Pleuritis can be a manifestation of Type II reaction.

Changes in testis and epididymis

Acute epididymo-orchitis is an important clinical manifestation of Type II reaction. It may be unilateral or bilateral the testes may be diffusely swollen and tender. Testicular atrophy may follow quickly either following acute orchitis or gradually following low grade orchitis. Gynaecomastia usually follows testicular atrophy.

Changes in breast

Acute mastitis can occur in females as a result of Type II reaction.

Changes in abdominal viscera

During Type II reation, the liver may be enlarged below the costal margin, become soft and very tender. Repeated lepra reaction can lead to persistent hepatomegaly, ascites, hepatic amyloidosis and splenomegaly.

Apart from microscopic changes observed in urine during Type II reaction, clinically renal involvement may manifest as glomerulonephritis causing frank hematuria and rarely causing oliguria. Repeated lepra reaction can lead to renal amyloidosis. Hypofunction of the adrenals and even frank peritonitis can occur during type II reaction.

Type III reaction (Lucio phenomenon)

Clinically, they start as painful red patches on the skin usually on one side of the limbs. They are ill defined and triangular or irregular in shape, later becoming purpuric and the centre becomes necrotic and ulcerated and finally develops a black or brown crust which falls off after a few days to leaving a superficial atrophic scar. Larger lesions on the legs are more inflamed, develop into bullae and burst leaving a deep ulcer with jagged edges which heals slowly if at all.

Rea and Levan[57] in their study, have found the reacting lesions to be most common on the legs, less commonly on the thighs, forearms and buttocks with sparing of trunk and face. These patients were afebrile throughout the course of the reaction.

COMPLICATIONS

Type I reaction

1. Sudden onset of paralysis resulting in claw hand (ulnar and median nerve involvement), foot drop (lateral popliteal nerve), facial palsy(facial nerve) and wrist drop(radial nerve).
2. Ulceration of the skin lesions

Type II reaction

1. Paralysis of involved nerves
2. Ulceration of the skin lesions
3. Blindness
4. Infertility
5. Perforation of the nasal septum and hard palate.
6. Secondary amyloidosis
7. Debility and exhaustion

Type III reaction

1. Secondary pyoderma and cellulitis
2. Secondary amyloidosis

HISTOPATHOLOGY

In all types of reaction, the onset is characterized by dermal edema histologically.

Type I reaction :

The onset of reaction is heralded by mild dermal edema. In the acute stages, there is profound dermal edema which causes disorganization and dispersal of the granuloma. In the early stages, the course of the reaction, whether upgrading or downgrading cannot be predicted. In upgrading reactions, there is increase in number of defensive cells such as lymphocytes, formation of giant cells and small clusters of epitheloid cells and decrease in number of bacilli.

If the reaction is of downgrading type, defensive cells are replaced by macrophages and there is increase in number of bacilli.

In severe reactions, necrosis may occur either in small foci or causing liquefaction of the entire granuloma and it is sometimes associated with local infiltration of polymorphonuclear leukocytes. There may be fibrinoid necrosis and finally fibrosis. As the reaction subsides, the granuloma takes on the characteristics of the position in the spectrum at which the patient was initially seen / had arrived. Biopsies of the skin lesion done prior to and after the subsidence of the reaction certainly aids in the distinguishing upgrading and downgrading reactions.

Type II Reaction :

Since it is a systemic reaction, in addition to the skin, the reacting granulomas may be found in nerves, lymph nodes, liver, muscle and synovia.

In the skin, the reaction is most often seen in the deep dermis or subcutis.

Histologically the reaction onset is characterized by edema of the papillary dermis, sharp influx of neutrophils and lymphocytes, evident as mixed dermal inflammatory infiltrates composed of neutrophils and lymphocytes superimposed on collections of foamy macrophages. The lymphocytes are mostly composed of CD4 cells and there is a decrease in numbers of CD8 T lymphocytes. Vasculitis of the nature of neutrophilic leukocytoclastic vasculitis affecting the arterioles or venules is a significant feature. Extravasated erythrocytes are often seen. Scanty fragmented and granular bacilli are seen around the vessels. Collections of small foamy histiocytic granuloma containing bacilli are seen scattered throughout the dermis and subcutis. The involvement of the subcutis is evident by mixed lobular and septal panniculitis. Direct immunofluoresence reveals deposition of IgG and C3 in the walls of the dermal blood vessels.

In a variant of ENL common to South East Asia, there is in addition to vasculitis, necrosis, involvement of the superficial dermis and epidermis & ulceration.

In another variant of ENL seen in Papua New Guinea, damage to collagen and elastic fibers of the dermis is the principal feature of the

reaction, which is a variable feature of ENL elsewhere. In the late stages, fibrosis is intense.

Lucio Phenomenon (Type III reaction)

Vascular changes are prominent features of this type of reaction but it differs from that seen in type II reaction.

There is endothelial proliferation in the medium sized vessels of the dermis and subcutis leading to thrombosis and associated infarction of the epidermis. There is a sparse largely mononuclear infiltrate with fewer neutrophils than in ENL. Sometimes there is prominent endothelial swelling and thrombosis of superficial vessels without a vasculitis. Dense aggregates of acid fast bacilli are found in the walls and endothelium of the normal appearing blood vessels as well as in the vessels with proliferative changes. Ischemic necrosis brought on by the vascular occlusion leads to hemorrhagic infarcts and results in crusted erosions or frank ulcers.

IMMUNOLOGY

Recent advances in the field of immunology have contributed to better understanding of various aspects of reactional states in leprosy.

Type I reaction

Type I reactions are acute inflammatory events usually occurring in borderline leprosy patients with immunologically unstable form of the disease. It is a delayed type hypersensitivity reaction (Gell and Coomb's

type IV hypersensitivity reaction) in which cell mediated immunity plays the major role.

Hypersensitivity can be defined as an expression of immune reaction in which the inflammatory response is very severe and out of proportion to the stimulus. The antigens released from the breaking down of M.leprae react with T-lymphocytes, initiating the reactional episode. The protein fraction of the organism tends to elicit a cell meditated immune response, while the polysaccharide portion elicits a humoral immune response.[33]

During the type I reaction, the antigens are located both in the skin and nerves. During the reaction in the skin, hypersensitivity is directed mainly against surface antigens, while during the reaction in the nerves, hypersensitivity is directed mainly against cytoplasmic antigens (Bryceson). Normally during leprosy, a delicate balance exists between the antigens available for immune reactions and the host response. Any alteration of this balance induces a reactional state.

The cell mediated immunity always tends to localize the disease as seen in tuberculoid and borderline tuberculoid leprosy. In such cases, only few bacilli if at all are detectable in the lesions by conventional staining methods. In cases of acute reactional episodes, mostly only degraded bacilli are visualized.

Reversal reaction

This condition is associated with a progressive increase in cell mediated immunity and destruction of the bacilli. Such a condition may occur either spontaneously or during and after completion of treatment. During successful treatment, the bacilli get fragmented. Each of these fragments act as antigens. They predict a progressive increase in cell mediated immunity and activation of T cells resulting in the acute reactional state.

However the reversal reaction may occur a long time after treatment cessation or disappearance of the lesions. (longest time reported is 16 years after successful treatment)[58]. This could possibly be because of persisters which had been inaccessible so far to organic defenses or drugs. These persisters could multiply later when conditions are favourable due to some intercurrent illness or immunological changes and initiate a new reactional episode[59]. Such late reversal reactions have been observed by investigators in the pre-sulfone era, who observed the natural history of some reactional cases and reported tuberculoid patients with reactions in which, the bacilli and the lesions resolved spontaneously following a reaction, only to reappear again after years of quiescence as erythematous lesions over previous sites with bacilli [60,61].

A study done by Shetty et al[62], who studied 25 patients of borderline tuberculoid leprosy, some of whom presented with late

reversal reactions occurring 1-13 years after release from treatment revealed viable bacilli in 58% of these patients (using foot pad of mouse culture)

In these cases, the cell mediated immune reaction could be related to the multiplication of the bacilli. The microorganisms thus destroyed release the antigens that give rise to a Type I reaction. If the number of bacilli is low, the patients become cured as the body defenses are able to deal with them. If the number of bacilli is high, there is a risk of new reactions, nerve involvement and disabilities.

The activation of T cells invariably occurs in cases of reversal reaction which is evidenced by ten fold increase of IFN – γ in these lesions. A four fold higher concentration of human gene serine factor (huHF), a marker for cytotoxic cells is also seen. Furthermore, infiltration of CD4 cells secreting IFN – γ and TNF – α in the skin and affected nerves is also seen with resultant edema and inflammation clinically[63]. T cells with γS receptors are also seen in large numbers reversal reaction[64]. γS T cells are important for granuloma formation observed in reversal reactions[64].

Reversal reactions are associated with a Th1 cytokine pattern with IL-2 and IFN – γ strongly expressed. The expression of inflammatory cytokines, in particular TNF – α is thought to be responsible for

pathological nerve damage associated with Type I reaction[65]. There is also an elevation of blood levels of these cytokines.[63]

It is also observed that IL – 6, IL – 10 and IL -13 are also present in the granuloma of the skin lesions of patients with type I reactions[66]. Pro inflammatory cytokines have a number of effects within the granuloma. They include a) promotion of protective cellular responses b) maintainence of granuloma formation[67] c) initiation of nerve damage[68]. In contrast the role of anti-inflammatory cytokines within the granuloma is not well understood. It can be postulated that the anti inflammatory cytokines play a crucial role in controlling the critical balance between the protective and tissue damaging effects of pro inflammatory cytokines[66]. The presence of both pro and anti inflammatory cytokines in these lesions highlights the multiplicity of cytokine expression within the granulomas of these patients and suggests that a simple model of Th1 activation is insufficient to explain the reactional pathology. This also highlights the complexity of regulatory pathways within the granuloma

Also observed are increased levels of neopterin either at onset of reversal reaction or 1 month thereafter, with levels declining on predninolme treatment[69]. There is also increased conversion of lymphocytes to lymphoblasts and increase in Langerhans cells in the skin[63]. This immunological upgrading can be evidenced clinically by a previously negative lepromin test becoming positive.

Downgrading reaction

This condition is associated with a reduction in cell mediated immunity, increase in number of bacilli and the appearance of new skin lesions. Such a situation occurs when the patient is not on treatment. The unhampered multiplication of the bacilli leads to a sudden increase in antigenic load, which is beyond the means of specific cell mediated immunity to cope up. Hence immunological downgrading results. This is evidenced clinically by a previously positive lepromin test becoming negative.

Type II reactions

This is an immune complex mediated syndrome where the humoral immunity plays the major role. This is an example of Coomb's and Gell type III hypersensitivity (Arthus phenomenon)

Type II reaction occurs in patients in borderline lepromatous (BL) and lepromatous (LL) spectrum of leprosy. It is rarely seen in histoid leprosy (only a few cases have been reported). In these patients, large amounts of mycobacterial antigens are available intracellularly in the macrophages and also in the intercellular spaces after release from these cells. A great majority of these patients also possess a high titre of precipitating antibodies in their serum. These antibodies lack any protective role. In non reactional states, they are unable to reach the intracellular organisms. The nature of this process which results in abrupt

release of antigen from the macrophages is not yet fully understood, and it is not yet certain whether the release of antigen is an immunological process or otherwise. However the release of mycobacterial antigens from the macrophages is required for formation and deposition of immune complexes which induce the acute tissue damage and typical clinical symptoms of ENL. It has recently been observed that the antibodies in patients with ENL react with distinct motifs R.G.D (arginine, lysine, aspartic acid)[38] which bind to fibronectin receptors of macrophages. These antibodies are mainly of IgG3 subclass[63]. There may be responsible for release of M.leprae antigens from the macrophages.

As already pointed out, it is the polysaccharide portion of M.leprae which is responsible for elicitation of the humoral immune response.

In ENL, the circulating antibodies contact the antigens across the vessel wall forming an Ag – Ab complex. The antigen antibody complex ratio is one of the many factors that determine the localization and deposition of immune complexes. ENL may be precipitated if the antigen – antibody ratio is balanced or if there is slight antigen excess. Complement is activated by the complexes and this attracts neutrophils whose lysosomal enzymes are responsible for much of the ensuing tissue damage. ENL is associated with a strong Th2 response with high expression of IL-4, IL-5 & IL-10. TNF – α concentration in the blood also rises to very high levels leading to systemic manifestations like

fever. Further the antibodies in Type II reaction are not specific against M.leprae. They cross react with cardiolipin and antigen of many different organs. In ENL, the immune complex have been demonstrated in renal glomeruli and ENL lesions[70,26,71]. Wemambu et al[71] found immunoglobulin and complement only in early ENL lesions and they reported that such deposits may not be found in specimens examined more than 24 hrs from their induction in laboratory animals. Circulating immune complexes have been described in this reaction[72] and its symptoms have been likened to those of chronic serum sickness. It has also been postulated that immune complex formation in ENL may occur extravascularly, as evidenced by increased concentration of complement split product C3 in the serum of patients with active ENL[25]. A report by Patnaik et al[73] attributed the exudative lesions seen in hepatic morphology during ENL to possible immune complex mediated mechanism. The eye and joint manifestations of ENL are also presumed to be due to immune complex mediated mechanism.

The immunological finding and the data supporting ENL as a typical immune complex mediated disease are contradicted by certain reports. Mshana et al[74] pointed out the failure to excite arthus reaction on intradermal injection of M.leprae antigens into a lepromatous leprosy patient. It has also been noted that there is a heightened T cell reactivity to M.leprae antigen and increase in numbers of T cells with increase in

CD4 / CD8 ratio upto two fold. CD8 T cells and cytotoxic T cells are reduced in number in skin lesions of ENL. Reversal of CD4 / CD8 ratio may be due to either marked increase in CD4 cells or decrease in CD8 T cells [74,75,76,]. The decrease in CD8 T cells may induce a change in the amount or affinity of the anti – M.leprae antibodies which favour the formation and deposition of immune complexes.

Another phenomenon observed in lesions of Type II reaction is a significant increase in apoptosis observed at 6 months of treatment[77]. Apoptosis is an active, self destructive cellular process and is considered an integral part of the repertoire available to the cell to respond to deleterious stimuli from within and without.[78] Apoptosis is the end point of an energy dependant cascade of molecular events and is regulated by several genes which induce p53, c-myc, Bcl-2, CED-3 and Fas genes.[78] Oliveira and colleagues found apoptosis to be greatly accelerated in circulating neutrophils in patients experiencing ENL.[79] The increased expression of pro apoptotic members of Bcl – 2 family of proteins and TNF – α in ENL is likely to induce more apoptosis. The greater bacillary load and type II reaction can also lead to increase in apoptosis.[77] The patho-mechanisms in Type II reaction may be much more complex and other immunological mechanisms may be involved as well.

The other serological abnormalities observed doing Type II reaction include positive tests for auto antibodies such as RA factor and ANA. There is an increase in circulating gamma globulins with raised levels of IgG, IgM, C2 & C3. The levels of c-reactive protein(CRP) also increases in the serum during the acute phase.

TYPE III REACTION (LUCIO PHENOMENON)

The immunological features of Lucio leprosy are same as in lepromatous leprosy with no evidence of cell mediated immunity against M.leprae. Most patients have high antibody activity against M.leprae and its antigens. Rea suggests that these patients have singularly deficient defense mechanism which permits unhindered multiplication of the bacilli in the vascular endothelium.

The immunology of Lucio phenomenon is believed to be based on Sanarelli Schwartzman reaction[80]. (non allergic but hypersensitivity phenomenon) where the basic pathology is due to unhindered multiplication of M.leprae in the vascular endothelium. The exposure of the bacterical antigens to the circulating antibodies results in vasculitis, proliferation of the vascular endothelium, thrombosis, infarction and necrosis of the overlying skin. But the histology of the lesion also suggests immune complex formation and deposition within the vessel walls so that it can be considered as a special variant of ENL in which the antigen is released mainly from the infected endothelial cells.

If the patients with Lucio phenomenon are given a lepromin skin test, they usually develop and extensive local reaction (The Medina – Ramirez reaction), occurring within 4-6 hrs and is a reproduction of the lesion in Lucio phenomenon.[22] Other immunological abnormalities seen in Lucio phenomenon are hyper gammaglobulinemia, cryoglobulinemia

of the mixed type consisting of IgG, IgM, IgA and complement components and positive VDRL tests for syphilis. Direct immunofluoresence reveals immunoglobulin and complement component in the vessel walls.

DIAGNOSIS

The diagnosis of reactional states in leprosy is mainly clinical. The following investigations could be contributory and useful for confirming the diagnosis under doubtful conditions.

Type I reaction :

Reversal reactions and downgrading reactions may sometimes appear similar and pose difficulties in diagnosis. They are not associated with any hematological or biochemical abnormalities. Sometimes it may be imperative to start steroids and study the response to differentiate them. The following investigations may be helpful in differentiating them:

Invivo tests :

1. Lepromin test
2. Skin biopsy

Invitro tests :

1. Lymphocyte transformation test
2. Lymphocyte stimulation test

The differences between reversal and downgrade reactions are:

		Reversal Reaction	**Downgrading Reaction**
1.	History	Pt. on treatment	Pt. not on treatment / irregular treatment / defaulter
2.	Clinical findings	a) No new lesions / few new lesions b) Ill defined lesions become well defined c) No extension in area of sensory deficit d) No new nerve involvement. Already involved nerves may be inflammed	a) More no. of new skin lesions b) Well defined lesions become ill defined c) Extension of area of sensory deficit present d) New nerve involvement present
3.	Bacterial index	Decreases	Increases
4.	Lepromin test	Negative tests revert to positive	Initially positive tests become negative / weakly positive
5.	HPE	Defensive cells such as lymphocytes, epitheloid cells and giant cells are increased. Bacilli decreased.	Defensive cells replaced by macrophages. Bacilli increased.

Type II reaction :

The diagnosis of type II reactions can be easily made on clinical grounds.

The various laboratory observed in Type II reactions are:

HEMATOLOGICAL

1. Hematological

Various hematological abnormalities can occur in type II reaction.

a) Leukocytosis : This can be very marked ranging from 20,000 to 50,000 cells / cu.mm and is predominantly neutrophilic.

b) Peripheral smear : Leukemoid picture with occasional myelocytes and normoblasts.

c) ESR : Usually markedly raised.

d) Thrombocytosis : Usually present.

e) Anemia : Normocytic normochromic anemia, megaloblastic anemia (due to sulpha drugs interfering with folic acid metabolism), aplastic anemia (due to drugs and toxins depressing the bone marrow) and hemolytic anemia (esp. in G-6PD def. individuals) can occur.

f) In severe reactions with hemolytic crisis, sudden profound fall in hemoglobin values and erythrocyte count is observed. Hemolysis will be echoed with a rise in reticulocyte count above 2%.

2. Biochemical

During the Type II reaction, abnormalities of Liver function tests have been reported. They include rise in SGPT and deficiency in coagulation factors. All these are due to moderate hepatic dysfunction and are reversible with the subsidence of the reaction. During severe

reaction with hemolytic crisis, mild rise in serum bilirubin (1-2mg%) has been observed. Alteration of albumin to globulin ratio is another biochemical change reported, [73] contributed mainly by increase in α – globulin.

3. Urine analysis

The urinary changes suggesting renal involvement in Type II reaction are albuminuria, (tract to 1 +), plenty of erythrocytes, pus cells and epithelial cells and presence of granular casts in urine. Also during the acute phase of type II reaction, traces of bile pigments can be found in urine. A patient in severe type II reaction can present with smoky urine due to hemoglobinuria. A persistent proteinuria following type II reaction should evoke the suspicion of renal amyloidosis.

4. Skin biopsy & histopathology

5. Fluorescent microscopy

Examination of early ENL lesions under fluorescent microscope will reveal deposits of IgG and C3 in the vessel walls.

Type III reaction (Luciophenomenon)

The usual laboratory findings are leukocytosis or absolute neutrophilia, anemia, high ESR, hypergammaglobulinemia and positive cardiolipin antigen tests for syphilis[22].

Histopathology and Direct immunofluorescence could confirm the diagnosis.

DIFFERENTIAL DIAGNOSIS :

Type I reaction :

1. Erysipelas
2. Urticaria

Type II reaction

1. Erythema nodosum leprosum

Other causes of erythema nodosum like tuberculosis, rheumatic fever and sarcoidosis should be excluded.. The features differentiating ENL and erythema nodosum of other causes are:

		ENL	**EN**
1.	Number	Numerous	Less numerous
2.	Site	Distributed all over the body including face	Less numerous usually limited to legs
3.	Nature of lesions	Evanescent	No evanescence
4	Diurnal variation	Appears usually in evenings	No diurnal variation
5.	Histopathology	Septal panniculits with foamy macrophages containing degenerating AFB in the dermis.	Septal panniculitis with dermis showing perivascular lymphocytic inflammatory infiltration in early lesions and lipid laden macrophages in late lesions with no AFB.

2. Bullous and pustular erythema nodosum leprosum

a) Erythema multiforme

b) Varicella

c) Rickettsial pox

d) Pustular psoriasis

e) Subcorneal pustular dermatosis

f) Pemphigus vulgaris

g) Bullous pemphigoid

h) Dermatitis herpetiformis

3. Conditions associated with primary panniculitis

Panniculitis secondary to infections, malignancy, vasculitis, pancreatic disease and Weber Christian disease.

4. Conditions associated with connective tissue diseases

a) Rheumatoid arthritis

b) Systemic lupus erythematosus

c) Scleroderma

d) Polyarteritis nodosa

5. Serum sickness

Type III reaction

1. Purpuric lesions

a) Henoch Schoenlein purpura

b) Pityriasis lichenoides et varioliformis acuta (PLEVA)

c) Cutaneous allergic vasculitis

d) Erythema elevatum diutinum

e) Diseases with dysproteinemia

2. Ulcerative skin lesions

a) Ecthyma and other pyodermas

b) Ischemic ulceration caused by underlying vasculitis

c) Dysproteinemic syndromes

d) Intravascular coagulopathy

e) Deep mycoses

f) Gummatous lesions

g) Lymphoma cutis & factitia.

MANAGEMENT

In the management of reactions in leprosy, a few general measures apply to all patients.

1. Patients in mild reaction, both Type I and Type II may be treated as ambulatory cases and severe cases must be hospitalized for treatment.

Bed rest to be reserved only for patients with severe reaction patterns and those with impending foot drop or other motor palsies.

2. To relieve the general constitutional symptoms, an NSAID like aspirin (600 – 200 mg 4-6 times daily), ibuprofen (200 – 400 mg TDS), or indomethacin (25-50 mg BD – TDS) can be given. In patients with mild constitutional symptoms, paracetamol (500 mg 4-6 times daily) may be sufficient.

3. To relieve the stress and anxiety, a tranquilizer / sedative may be prescribed.

4. Investigations for the presence of intercurrent infections or other precipitating factors should be carried out.

5. Reassurance & counseling is particularly important because the patient's first assumption is that his disease is not responding to conventional treatment and is getting worse. Some patients may even discontinue antileprosy drugs or may go for native medicines. They can be assured that they are recovering their lost immunity and the disease is getting eliminated.

6. Anti leprosy therapy : Though much controversy had prevailed in the past about the continuation of antileprosy therapy (esp. dapsone) during reaction, the present view is that it should be continued in full dose during the reactions also with following hints of caution:

a) In patients who present for the first time with severe neuritis, dapsone may be replaced by clofazamine and thiambutosine, along with NSAIDs and steroids.

b) Some patients with borderline leprosy go in for severe reactions within a few weeks after initiating MBMDT. Previously when dapsone monotherapy was practiced, it was replaced by clofazamine. Nowadays with the advent of MBMDT, it is no longer imperative to withdraw dapsone. However in case of severe uncontrollable and steroid dependant reactions, dapsone may be withdrawn temporarily, which may allow steroids to be withdrawn later.

ANTIREACTION DRUGS

1. Corticosteroids

Corticosteroids form the mainstay of management of both Type I and Type II reactions in leprosy. In managing reactions, early intervention is crucial if permanent nerve damage is to be avoided and impairment of function is to be reversed. Corticosteroids are the only drugs known which can quickly reverse the inflammation and help in restoring function.

In 1950, Chaussinand in his textbook ‘La Lepre’ first mentioned about the use of cortisol / ACTH in the treatment of Type I reaction. Thereafter it was incorporated and brought into general use for the

treatment of Type I & Type II reactions. It action in Type I and Type II reactions is by virtue of its anti-inflammatory and immunosuppressive properties.

Hence steroids cause inhibition of both early and late phases of inflammation. The preferential depletion of CD4 T cells and B helper cells (those with Fc receptors for IgM) result in normalization of disturbed helper suppressor T cell ratio as seen in erythema nodosum leprosum. These compounds also have been found to prevent and control adjuvant arthritis possibly due to redistribution of T cells.

Dose : T.Prednisolone 40 – 80 mg / daily, which is gradually tapered.

It can however cause adverse effects like exacerbation of acid peptic disease, growth impairment in children, HPA axis suppression, hypertension, hyperglycemia, reactivation of latent infections, etc and its use is to be governed by strict supervision.

2. Thalidomide

Thalidomide or α – (N phalimido) glutarimide was first developed in 1954 and marketed in 1957 for use as sedative / antiemetic in pregnant women. In the early 1960s its teratogenic potential was identified and the drug went out of market in 1961. In 1965, Sheskin reported the effectiveness of thalidomide in the management of ENL[82].

Thalidomide is a racemic glutamic acid analogue composed of two enantoimers R – and S- Thalidomide, which interconvert under physiologic conditions. The two enantiomers have differing properties; one is a more potent suppressor of TNF release by stimulated blood mononuclear cells while the other is sedative[83.] Thalidomide undergoes hydrolysis at pH 7.0 resulting in the formation of more than 20 products, which are responsible for the activity. It is effective only in Type II reaction.

It is anti-inflammatory in nature and acts by inhibiting the release of TNF, IFN – α, IL-10, 12, cyclo-oxygenase and NF-kB. It also decreases the effect of complement derived chemotactic factors resulting in reduced or non recruitment of polymorphonuclear leukocytes into the lesions. It is also said to result in improvement of motor conduction velocities of nerves involved in erythema nodosum leprosum.

Dose : Initial : 100 – 300 mg / day in divided doses

Maintenance : 50 mg / day

It results in teratogenicity (phocomelia) if the drug is taken between 35^{th} – 50^{th} day post LMP. It also causes drowsiness, sedation and irreversible peripheral neuropathy.

3. Clofazamine (Lamprene)

This red immunophenazine dye was first discovered by Dr. Vincent Barry in his laboratory in Dublin and it was Dr. Stanley Browne who first used it clinically in leprosy. It is a part of the multibacillary drug regimen for leprosy.

It is useful in patients with Type II reaction and those with severe Type I reaction, who have become steroid dependant[85]. It decreases neutrophil chemotaxis with consequent decreased influx of polymorphs into the inflamed area[85]. It decreases antibody formation, with consequent control and prevention of reactions[85]. It also increases synthesis of lysosomal enzymes and enhances phagocytic ability of macrophages, resulting in complete digestion of antigens or degradation of antigens to less antigenic forms[85].

The drug is, however very slow to act taking weeks for its full effect indicating the need to add other drugs for the management of acute / subacute manifestations. The drug has only a limited role in neuritis since it takes too long for any significant effect. The usefulness of this drug lies in its being primarily an anti-leprosy drug being helpful in management of chronic recurrent erythema nodosum leprosum as also in with drawing steroids in steroid dependant cases.

Dose : Initial : 300 – 400 mg / day

Maintenance : 100 mg/ day

1. It can cause certain undesirable adverse effects including reddish brown pigmentation of the skin, conjunctiva, body secretions & feces, brownish corneal deposits and retinal spots, ichthyosis and pruritus. It can also cause photosensitivity and eosinophilic enteritis.

4. Chloroquine

It is a 4 aminoquinoline derivative used as an antimalarial drug. It is used primarily in reactions in leprosy due to its antiinflammatory nature. It is useful in mild Type I reaction, where ulceration and neuritis do not occur and for mild to moderate ENL without complications.

Dose: Initially chloroquine is given in a dose of 250mg thrice daily for the 1st week, 250mg twice daily for the 2nd week and 250mg once daily thereafter. 250 mg OD on alternate days is sufficient to maintain control.

It can cause gastrointestinal upset, hemolytic anemia, blurred vision, hypertension, cardiovascular collapse, lichenoid dermatitis, flare up of psoriasis and bleaching of hair and moustache.

5. Antimonials :

With the advent of conticosteroids, thalidomide and clofazamine in the treatment of lepra reactions, antimonials are less frequently used because they are less effective and more toxic. Potassium antimony

tartrate and stibophen are examples of this group of drugs. The former can be used only intravenously and the latter is given intramuscularly. No oral preparations are available. They are particularly useful in relieving the pain in bones & joints in Type II reaction and for mild type I reaction, where neuritis and ulceration do not occur.

Dose: Potassium antimony tartrate : The usual dose is given as 0.5 – 1% solution I.V. This is repeated every other day. The dose may slowly be raised from 20 to 60 mg based on the clinical response. The total dose should not exceed 500-1000 mg. If no response is seen by 6^{th} dose, it is unlikely to be effective and the drug is withdrawn.

Stibophen: The initial dose is 1.5 ml i.m and if no adverse reaction occurs, 3.0 ml is given 2 days later followed by 3-5 ml on alternate days. The total dose should not exceed 30 ml and if no response is seen by 6^{th} dose, it is withdrawn.

The courses of both potassium antimony tartrate and stibophen may be repeated if necessary after an interval of several weeks.

However, there is a risk of severe anaphylactoid reactions, pneumonia, joint & muscle pain, acute arthritis, hepatitis, renal damage and cardiac toxicity.

6. Colchicine

It has been found to be useful in Type II reactions, particularly in frequent or recurrent severe ENL reactions. In a dose of 1.5 – 2 mg daily

in divided doses[86], it is reported to have dramatic effects in controlling fever and erythema nodosum leprosum. It is also indicated in the treatment of amyloidosis secondary to chronic skin ulceration[22] and has prophylactic value in patients without amyloidosis. It probably owes its effectiveness to its ability to inhibit neutrophil chemotaxis. This drug also restores T cell balance[85].

7. Zinc

This drug is under extensive trial. It is recommended in treatment of erythema nodosum leprosum and chronic leg ulceration resulting from necrotic ENL lesions. It is reported to have inhibiting effect on neutrophic chemotaxis and complement mediated reactions. In a study by Mathur et al[87], out of 8 patients with ENL treated using oral zinc sulphate, steroids could be withdrawn completely in 7 patients with reduction in weekly dose of clofazamine and better tolerance of dapsone. The recommended dose is 220 mg TDS.

8. Azathioprine

It has been reported to be effective in the management of severe or refractory Type II reaction[88,89]. The recommended dosage is 50 mg/day. It reduces sythesis of TNF – α, thus serving as a potent anti-inflammatory agent. It also appears to be safe during pregnancy[90].

9. Methotrexate

Methotrexate also is useful in treatment of severe and refractory ENL[91]. But it is highly teratogenic and both men and women are advised to avoid planning pregnancy while on methotrexate and for 6 months after stopping it.

10. Mycophenolate Mofetil

It has been reported to be useful in treatment of erythema nodosum leprosum. Mycophenolate mofetil is the prodrug of mycophenolic acid, which is a potent inhibitor of type II isoform of inosine monophosphate dehydrogenase, which is expressed in activated T & B lymphocytes. Its efficacy is mainly due to induction of apoptosis of activated T cells[92], eliminating clones of cells responding to antigenic stimulating[92]. Depleting guanosine nucleotides, it also suppresses glycosylation and expression of some adhesion molecules. It also depletes tetrahydrobioterin, which is a cofactor for inducible form of nitric oxide synthetase – iNos[92]. It is used in a dosage of 0.5gm twice a day with dose reduction over 4-6 months and further followed for another 2 months[92]. It is useful as a steroid sparing agent and in patients in whom systemic steroids are contraindicated.

11. Pentoxyphylline

It is a methylxanthine derivative with potent haemorrheologic properties used for intermittent claudication and chronic leg ulcers. It also

has immunomodulating effect due to suppression of monocyte production of TNF – α and IL-1[93]. It is hence useful in Type II reactions in leprosy. It is useful to some extent in a dose of 1.2gm daily[91].

12. Cyclosporine – A

The role of cyclosporine in ENL was thought to be promising following invitro studies, but however relevant clinical data are lacking[91]. It was first tested invitro using peripheral blood mononuclear cells from ENL patients. It was found that lepromin induced Con-A suppression of suppressor cells was reversed with predominant effect on adherent cells[85]. It was found useful in a small series of 3 patients, when given in a dose of 100-200 mg daily[85]. The limiting factors were GIT symptoms observed in all three patients.

13. Levamisole

Some reports are available in literature which state levamisole has been useful in ENL cases. However the results have not been encouraging. The possible consideration for its use was its ability to restore T cell numbers to normal[85].

14. Aspirin and Indomethacin

Aspirin has been evaluated in the treatment of ENL in three double blind controlled trials and indomethacin in one. Both were found less effective than thalidomide and prednisolone. In one study, aspirin was

compared with colchicine in the management of ENL and both were equally effective in mild disease[94].

15. Trepterygium Wilferdin hook – A Chinese Herb

This herb has been reported to be effective in both Type I and Type II reactions, with efficacy of 96.6% and 98% respectively[85]. This herb is also effective in suppressing neuralgia.

16. Plasmapheresis

This method has been employed in treatment of both type I and type II reactions[85] and involves replacement of plasma of the patient with sterile albumin solution. It has been suggested that type I reaction is on account of appearance of some plasma factors that augment LTT response of lymphocytes. The removal of this immunostimulatory factors results in beneficial effect by reducing the hypersensitivity response[85]. It also has been seen to be effective in ENL. Its possible mechanism includes dilution of cytokines, free antigens and antibodies[85].

17. Zafirlukast

This leukotriene antagonist has been tried in an open phase II cohort trial using an initial dose of 40 mg twice daily. It was effective in six patients with ENL although outcome measures were not defined[95].

18. Infliximab

The successful use of this chimeric monoclonal antibody, which suppresses the biological activity of TNF by specifically binding to it has been reported in a single case of recurrent ENL treated in Netherlands[96].

MANAGEMENT OF Type I REACTION

The 7th WHO expert committee on leprosy stated in June 1997[97] that the crucial elements in the management of leprosy reactions and thereby the prevention of disabilities are early diagnosis of reactions together with prompt and adequate treatment. Corticosteroids are the sheet anchor of treating reversal reactions. Mild reactions without neuritis can be adequately managed using aspirin and chloroquine. WHO states that for severe reactions and neuritis less than 6 months, the recommended dose of prednisolone is 40-60 mg daily, gradually reduced and tapered weekly or fortnightly and stopping after 12 weeks[98]. All patients with recent nerve function impairment < 6 months duration demonstrate greater improvement in nerve function than those with old impairments[98].

WHO regimen is clearly very short in which the prednisolone dose stayed above the crucial dose of 15-20mg only during the first 2-3 months. Some authors however have stated that such a short treatment could not be effective in the long run[81]. Researchers at All Africa Leprosy

and Rehabilitation Training Centre (ALERT) have used a regimen consisting of T.prednisolone 30-40 mg once daily, which after 1 month was reduced over a 2-3 months period to 20—25 mg. Thereafter prednisolone was decreased by 5 mg once a month. The dose was increased again to the previous dose when nerve function parameter deteriorated. It was noted that 15-20 mg was the critical dose of prednisolone required to control a reversal reaction after the initial period. The total treatment duration was 4-9 months for BT patients, 4-14 months for BB patients and 6-20 months for BL patients. A study by Li Huan Ying[99] reporting on the duration of reversal reaction, states that only 39.6% of reactions subsided in less than 3 months and 62.1% within 6 months. In 22.2% of BL patients it was found that reversal reaction lasted at least 7-12 months. Other evidence supporting prolonged treatment with prednisolone was recently reported by Little et al[100], who observed that there was a continuing Th1 cytokine activity even 180 days after start of prednisolone in some of the patients at follow up. At the 16th International Leprosy Congress in Salvador, Bahia, Brazil, P.S.Rao presented a controlled trial of different prednisolone dosages and durations in type I reactions based on a protocol written by Lienhardt, which showed clearly that the longer duration was statistically better than the shorter duration, but the initial dose (60 mg compared to 30 mg) was not significant[81]. A

treatment proposal by Ben Naafs[81] is as follows with T. prednisolone once daily in the morning.

Paucibacilary	**Multibacilllary**
40 mg 2 wks	30 mg 1 month
30 mg 2 wks	25 mg 2 months
25 mg 1 month	20 mg 3 months
20 mg 2 months	15 mg 2 months
15 mg 1 months	10 mg 2 weeks
10 mg 2 weeks	5 mg 2 weeks
5 mg 2 weeks	
Total – 6 months	Total – 9 months

The use of high dose corticosteroids is not without adverse effects, which are very common. Hence patient monitoring is considered very important. The following parameters are taken into account:

a) Monitor blood pressure and weight at each visit
b) Urine analysis & blood glucose estimation
c) Gastric protection with H2 blocker or proton pump inhibitor.
d) Treat those at rise of strongyloides stercoralis with albendazole / ivermectin
e) Osteoporosis prevention.

Immunosuppresants like azathioprine are also said to be effective in type I reactions. Azathioprine in combination with an 8 week course of prednisolone was as effective as a 12 week course of prednisolone alone in the management of type I reactions in a pilot study done in Nepal[101].

Antileprosy drugs

If the patient is on treatment with dapsone at the time of reaction, it is generally continued at its full dose. In case the patient is not on dapsone at the onset of reaction it can be started after the reaction is brought under control. In ALERT dapsone was discontinued for the first 2 weeks of antireaction treatment thereafter restarted and continued at its full dose.

Neuritis

The various modalities of management of neuritis are:

a) NSAIDs
b) Anti reaction drugs esp. corticosteroids which cause dispersion of intraneuronal edema.
c) Suitable supportive therapy for paralysed muscles in the form of padded splints. Sessions of graduated passive and active exercise will aid muscle recovery and prevent stiffness of joints.
d) Intraneural injections – This can be given for relief of severe nerve pain. A combination of 1500 units of hyaluronidase, 1 ml of 2% lignocaine and 1 ml of hydrocortisone suspension containing 25

mg/ml is injected into the swollen nerve or around it using 14 size needle after infillrating the skin with local anaesthetic agent.

e) Surgical treatment : - Surgery also finds a role in the management of neuritis, esp that of ulnar neuritis, but also of other nerves as well. The various surgical procedures include nerve decompression (neurolysis), decompression with transposition and decompression with epicondilectomy. The indications for nerve decompression are:

    a) Severe intractable pain
    b) Nerve abscess
    c) Recurrent neuritis
    d) Increased weakness of muscles and impending paralysis
    e) Cases not responding to medical management within 4 weeks[102].

Downgrading reaction

This is usually managed by continuation of appropriate antileprotic therapy. For patients with neuritis or marked erythema or edema of skin lesions, a brief course of corticosteroids may be beneficial.

MANAGEMENT OF Type II REACTION

There are three patterns of erythema nodosum leprosum, which was identified in a cohort of 82 Indian patients. They are acute single

episodes, recurrent acute episodes and chronic ENL[91]. Acute single episodes were defined as a single episode responding to steroid treatment and accounted for only 6% of the episodes. Recurrent acute episodes comprised recurrent episodes with periods off all treatment. It comprised 32% of all case types. It was termed chronic when patients needed steroid treatment for more than 6 months. It accounted for 62% of all case types[91]. In 1998, WHO expert committee on leprosy report discussed the management of Type I (reversal) reactions and ENL together[103] advising that severe ENL can be treated with prednisolone, as for reversal reaction (a 12 week course), with the maximum dose not exceeding 1mg/ kg body weight. The ILEP technical bulletin on the management of ENL recommends treating severe ENL with corticosteroids at a starting dose of 30-60mg and reducing every week by 5-10mg. It states that a maintenance dose of 5-10mg may be needed for several weeks to prevent recurrence of ENL[104]. When clofazamine is used at a dose of 300mg, WHO expert committee recommends that the drug should not maintained at this dose for more than one year.[103] On use of thalidomide, WHO expert committee advises that it should be given only to men or post menopausal women who are dependant as corticosteroids.[103] ENL can be managed as given below:

Mild reactions

a) Aspirin (or) paracetamol

b) Sedatives

c) Chloroquine 250mg TDS x 2 weeks

Moderate reaction

a) Sedatives

b) Aspirin 300mg TDS or as necessary

c) Chloroquine 250mg TDS (till fever subsides)

d) Prednisolone 20-40mg daily, tapered off in 4-6 weeks.

e) Previously, Sodium antimony gluconate was given : 20mg in alternate days x 3 – 6 doses.

Severe reaction

a) Rest, analysis, sedatives

b) Prednisolone 40-60mg / day, tapered off in 4-6 weeks

c) Previously,thalidomide was given.

d) Clofazamine 100mg TDS initially, then tapered to 50mg daily

e) In case of severe recurrent erythema nodosum leprosum, pulsed intravenous corticosteroids have been tried once monthly along with azathioprine in a dose of 50mg daily by Mahajan et al[105].

f) Management of complications.

In case of severe recurrent chronic erythema nodosum leprosum pulsed intravenous corticosteroids along with azathioprine 50 mg daily can be tried as suggested by Mahajan et al[104]

Type III rection (Luciophenonenon)

Mild cases : Self limiting

Moderate to severe cases : Steroids are moderately effective. To start with atleast 60mg prednisolone should be given daily which can be tapered off over several weeks. Thalidomide and clofazamine are ineffective. All therapy including immunosuppressants are ineffective. Plasmapheresis is reported to be effective.

AIMS AND OBJECTIVES

1. To find out the age and sex incidence of different types of reactional states in leprosy.
2. To study the incidence of different types of reactions occurring across the spectrum of leprosy.
3. To study the onset of reaction in relation to duration of disease and initiation of treatment and the frequency of exacerbations..
4. To study the different signs and symptoms associated with Type I and Type II lepra reactions.
5. To study the clinical and histopatholoical correlation of Type I and Type II lepra reactions.

MATERIALS AND METHODS

Fifty patients presenting to the leprosy out patient department with any type of lepra reaction between August 2008 and July 2009 were included for the study. This included both old and new cases. As per WHO recommendation, patients with multibacillary disease are treated for 12 months and those with paucibacillary disease are treated for 6 months. All patients presenting with reaction, including those who are already on antileprosy drugs and new patients seeking medical attention for the first time were included in the study. A detailed case proforma was prepared for each patient which included the patients' demographic details, detailed history, time of starting MDT, regimen followed and time of stopping MDT. The clinical features were noted and the clinical type of leprosy and the type of leprosy reaction was assessed. The time of developing leprosy reaction, recurrence of reaction within 6 months, neurological symptoms and signs including nerve tenderness, pain, new disability were all noted down carefully. Initial bacteriological index was estimated and a biopsy and histopathological study was done for all the patients. Other investigations including complete blood count, renal function test, liver function test, serum electrolytes, X-ray chest and smear for MP/MF was also done.

Definition of Leprosy reaction

Type I reaction was diagnosed if existing skin lesions became inflammed or if the patients developed nerve tenderness and new nerve functional impairment (sensory or motor). Type II reaction was diagnosed if the patient developed crops of erythematous tender nodules (erythema nodosum leprosum) with the presence of any of the following : fever, malaise, peripheral nerve pain or tenderness, joint pain, lymphadenitis, iridocyclitis or orchitis. If the patients had nerve pain, nerve thicknening or nerve tenderness, they were diagnosed as neuritis. Grading of both Type I and Type II reactions was also done.

Treatment and followup

Type I reaction, including neuritis was treated using analgesics, chloroquine, antibiotics and a standard 12 week course of steroids as recommended by WHO with a starting dose of 40mg / day. Type II reaction was also treated using the same dose of T.prednisolone 40mg / day tapered gradually once in two weeks. Clofazamine was used in two patients and pentoxyphylline in one patient who had repeated exacerbations and could not be weaned from steroids. All the patients were followed up for a minimum period of 6 months.

RESULTS

A total of fifty patients were included in the study. There were 30 patients with Type I reaction and 20 patients with Type II reaction. There were no patients with Type III reaction.

The mean ages of patients with Type I and Type II reactions were 39.83 yrs and 37.45 yrs respectively. 25 (50%) of the patients in either reaction were found in the age group of 21- 40 years. 13 (26%) were aged above 50 years, 8 (16%) were between 41 – 50 years and only 4 (8%) were less than 20 yrs old, the youngest patient being a boy 15 years of age. (Table 1, Figure 1)

There were a total of 34 male patients and 16 female patients, with a sex ratio of 2.12. The sex ratios of patients with Type I and Type II reactions were 1.3 and 4.0 respectively. Thus male patients constituted 68% of the total number of cases.

Out of the 30 patients with Type I reaction, 28 were upgrading and two were downgrading (Figure 3). It was also noted that out of 28 patients in Type I upgrading reaction, 26 (92.85%) were primarily diagnosed as borderline tuberculoid Hansen's disease and the remaining 2 (7.15%) as borderline lepromatous Hansen's disease. Among the 2 patients with downgrading reaction, 1 was diagnosed with borderline tuberculoid

TABLE 1: AGE AND SEX INCIDENCE OF TYPE I AND TYPE II REACTIONS

Age (years)	Total no.of cases	No. of male	No. of female
<10			
11-20	4	3	1
21-30	12	10	2
31-40	13	8	5
41-50	8	4	4
>50	13	9	4

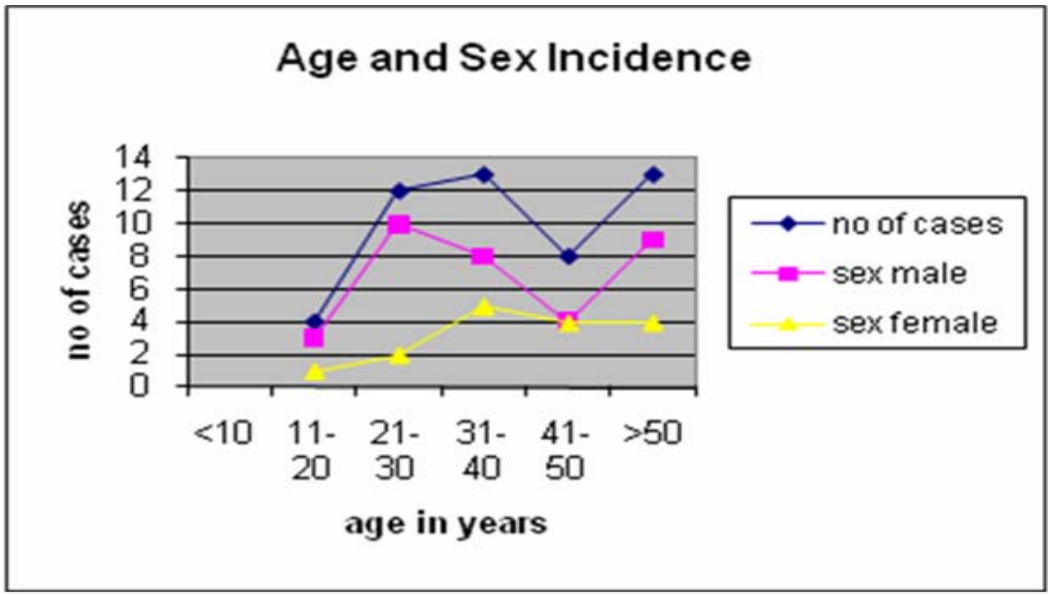


FIGURE 1

TABLE 2: INCIDENCE OF DIFFERENT TYPES OF REACTIONS OCCURRING ACROSS THE SPECTRUM OF LEPROSY

	Different types of reactions		
Type of leprosy	**Type I upgrading**	**Type I downgrading**	**Type II**
BT	26 (92.85%)	1 (50%)	0
BB	0	1 (50%)	0
BL	2 (7.15%)	0	4 (20%)
LL	0	0	13 (65%)
Histoid	0	0	3 (15%)

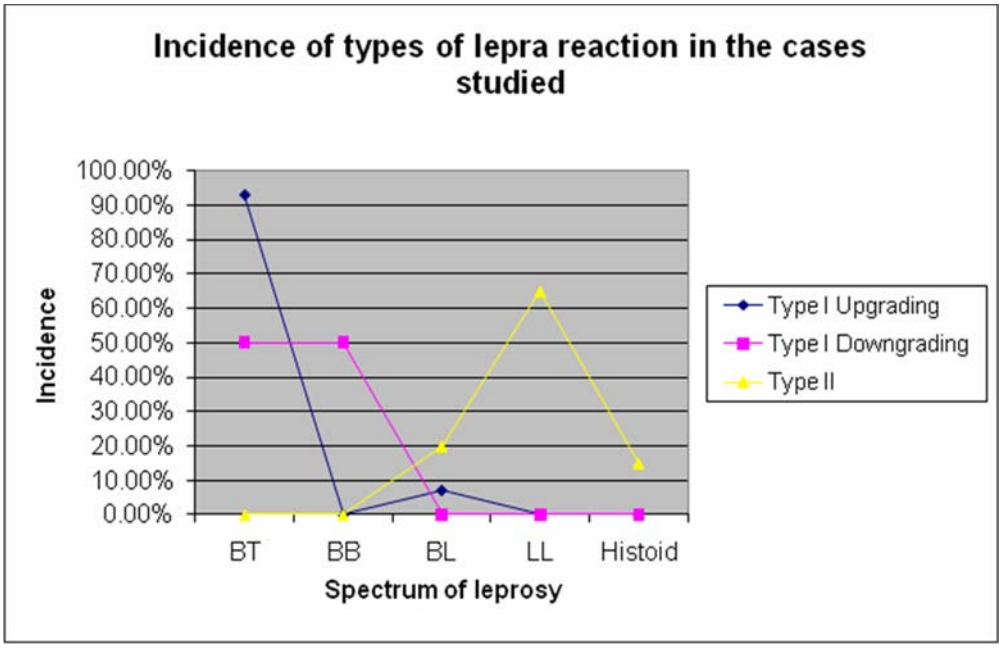
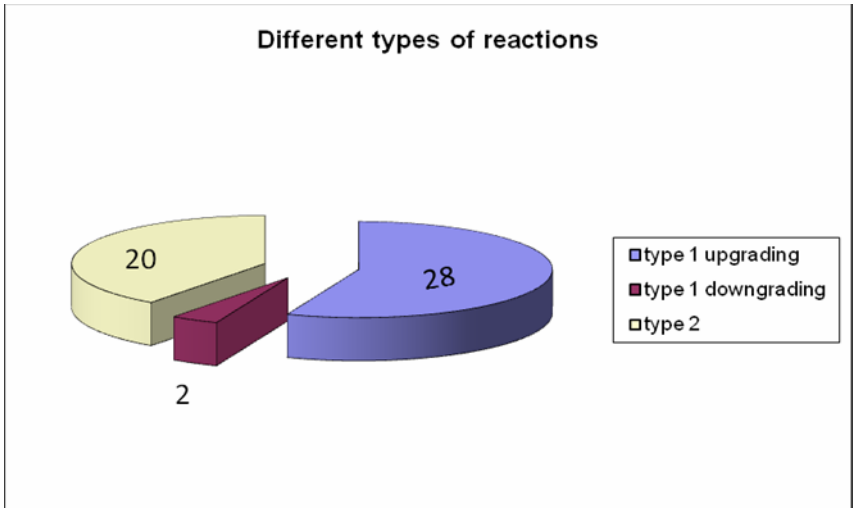


FIGURE 2

Onset of reaction in relation to initiation of treatment	Type I reaction	Type II reaction
Started with reaction	12 (40%)	2 (10%)
< 6 months	3 (10%)	4 (20%)
6 months – 1 year	3 (10%)	0
1-3 years	7 (23.33%)	6 (30%)
3-5 years	4 (13.33%)	6 (30%)
> 5 years	1 (3.33%)	2(10%)



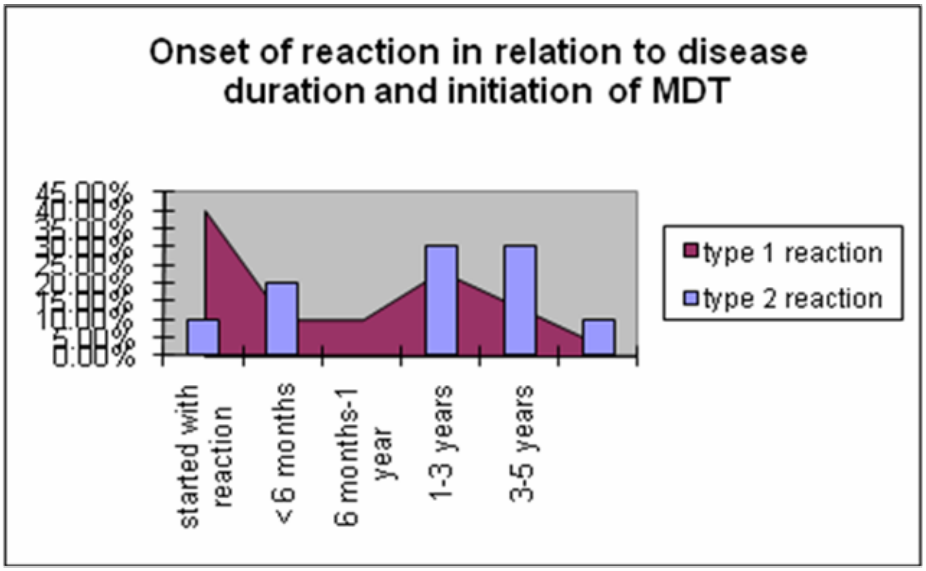


FIGURE 4

TABLE 4: CLINICAL FEATURES

Clinical features	Type I reaction	Type II reaction
Fever	5 (16.66%)	20 (100%)
Arthralgia	1 (3.33%)	14 (70%)
Oedema of extremities	10 (33.33%)	17 (85%)
Oedema of face	2 (6.66%)	7 (35%)
Lymphadenitis	0	8 (40%)
Epistaxis	0	10 (50%)
Orchitis	0	2 (10%)
Iritis	0	1 (5%)
Neuritis	14 (46.66%)	8 (40%)
Claw hand	4 (13.33%)	2 (10%)
Foot drop	2 (6.66%)	1 (5%)
Facial palsy	1 (3.33%)	2 (10%)
Ulceration of skin lesions	0	2 (10%)
Exacerbations	13 (43.33%)	15 (75%)

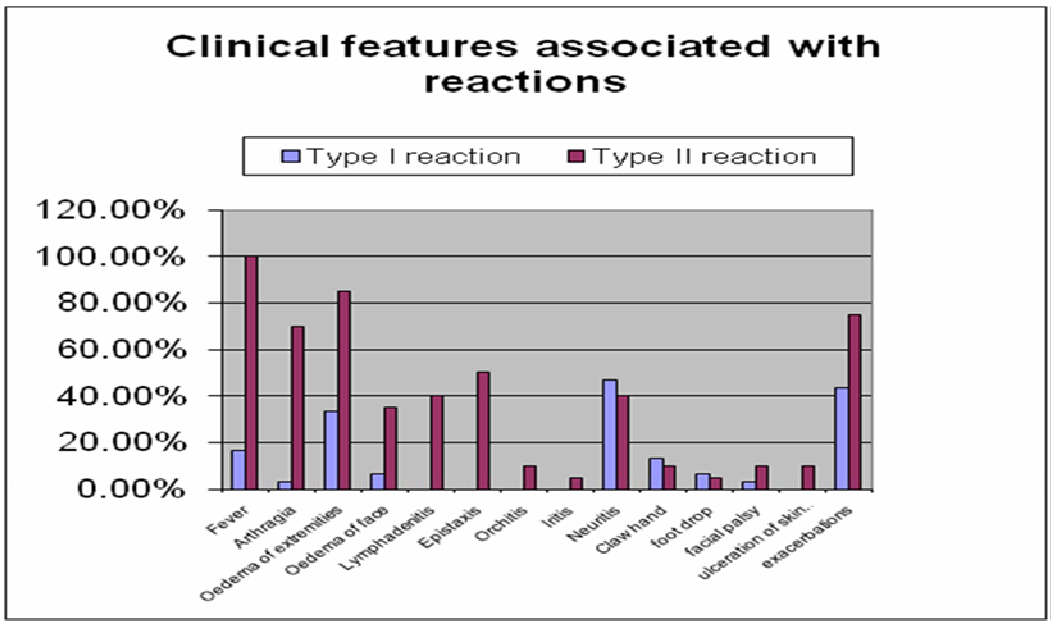


FIGURE 5

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TABLE 5: GRADING OF REACTIONS

Severity of reaction	Type I reaction	Type II reaction
Mild	16 (53.33%)	2 (10%)
Moderate	5 (16.66%)	11 (55%)
Severe	9 (30%)	7 (35%)

owngrading to mid borderline and the other patient with mid borderline downgrading to borderline lepromatous leprosy. Among the 20 patients who developed type II reaction, 13 (65%) of them were primarily diagnosed with lepromatous leprosy. Four patients (20%) belonged to the borderline lepromatous spectrum and the remaining 3 (15%) were diagnosed to have histoid leprosy.(Table 2, Figure 2)

It was observed that among the 30 patients with Type I reaction, 12 (40%) presented with reaction before initiation of MBMDT (Multibacillary Multidrug therapy). Three patients (10%) developed Type I reaction within 6 months of starting MBMDT and 3 (10%) developed the reaction after 6 months. Seven patients (23.33%) developed Type I reaction between 1-3 years after initiation of therapy and 4 (13.33%) developed the reaction between 3-5 years after starting therapy. Only 1 patient (3.33%) developed the reaction after 5 years of therapy. Among patients with Type II reaction, 2 (10%) presented with reaction before diagnosis and initiation of MBMDT and 4 (20%) developed the reaction within 6 months of initiation of therapy. Six patients (30%) each presented with reaction between 1-3 years and 3 -5 years after initiation of therapy. Only 2 patients (10%) developed Type II reaction 5 years after initiation of therapy. (Table 3, Figure 4)

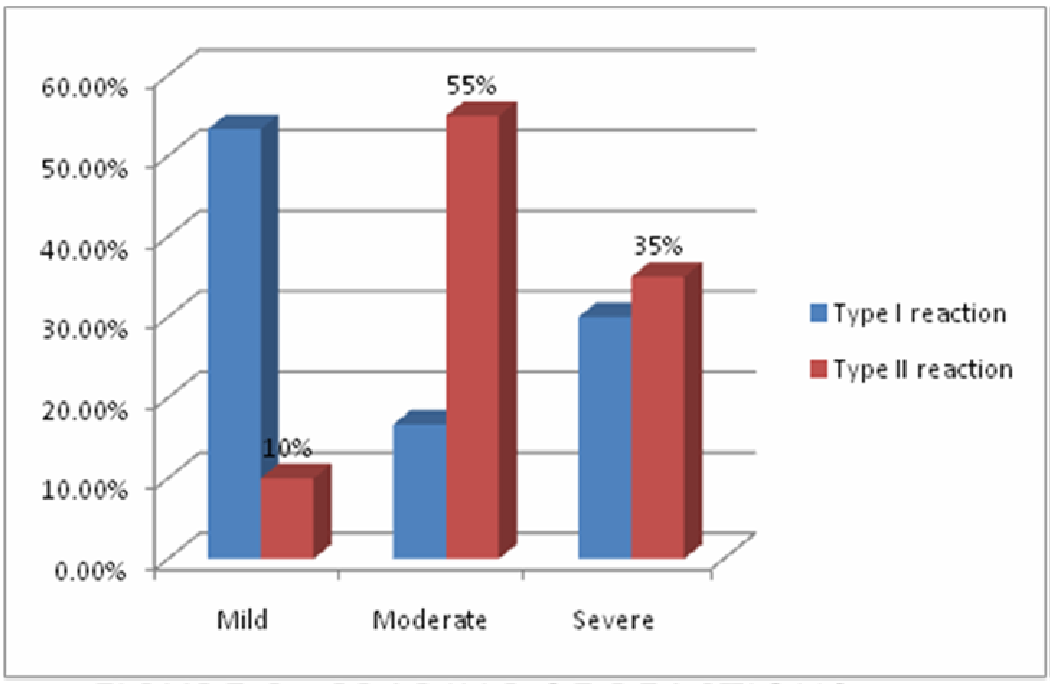


FIGURE 6 : GRADING OF REACTIONS

TABLE 6 : EXACERBATION OF REACTIONS

Exacerbation of reaction	Before 12 weeks	After 12 weeks	Total
Type I reaction	3 (23.07%)	10 (76.93%)	13 (43.33% of total)
Type II reaction	10 (66.66%)	5 (33.34%)	15 (75% of total)

Apart from the raised erythematous skin lesions which were found in all the patients, neuritis was the predominant feature in Type I reaction. It was seen in 14 (46.6%) patients. Ulnar nerve and lateral popliteal nerve were seen to be predominantly involved. During the time of reaction, deformities like claw hand, foot drop and facial palsy was seen in 4 (13.3%), 2 (6.6%) and 1 (3.3%) patients respectively. Fever was seen only in 5 (17%) patients. Oedema of the extremities were seen in 10 (33.3%) of the patients. In patients with type II reaction, fever was noted in all the patients, arthralgia in 14 (70%), oedema of the extremities in 17 (85%), oedema of the face in 7 (35%), neuritis in 8 (40%), iritis in 1 (5%), orchitis in 2 (10%) and lymphadenitis in 8 (40%) patients (Table 4, Figure 5). Among patients with Type I reaction, 16 (53.33%) had mild form of reaction, 5 (16.66%) had moderate form and 9 (30%) had severe reaction. Among patients with Type II reaction, 2 (10%) had mild form, 11 (55%) had moderate form and 7 (35%) had severe form of reaction. (Table 5,Figure 6)

During the follow up, exacerbation of Type I reaction was seen in 13 (43%) patients. Among these 13 patients, 10 (76.93%) of them had exacerbations after 12 weeks of WHO recommended regimen. The rest of them (23.07%) had exacerbations within the 12 week period when the dose of steroids was being tapered. Among these 13, 6 (46.15%) had

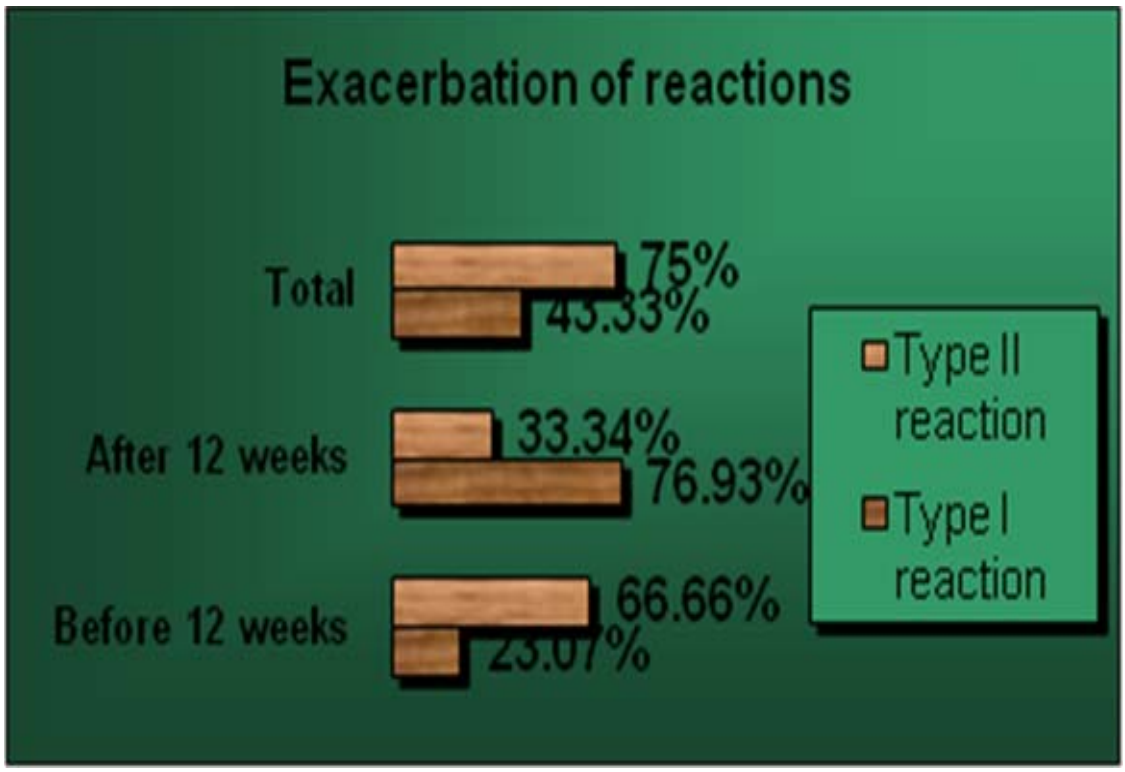


FIGURE 7

TABLE 7: BACTERIOLOGAL INDEX

BI	Type I reaction	Type II reaction
Smear negative	26 (86.66%)	5 (25%)
<=1	4 (13.33%)	1 (5%)
2-3	0	5 (25%)
>=4	0	9 (45%)

Histopathological changes	Type 1 reaction	Type 2 reaction
Epidermal changes	12 (40%)	15 (75%)
Grenz zone	-	16 (80%)
Dermal edema	22 (73.33%)	16 (80%)
Epitheloid granuloma	30 (100%)	-
Infiltrate in dermis	-	10 (50%)
Infiltrate in dermis + subcutis	-	10 (50%)
Neutrophilic abscess	-	10 (50%)
Vasculitis	-	10 (50%)
Panniculitis	-	10 (50%)
Fragmented AFB +ve	-	16 (80%)

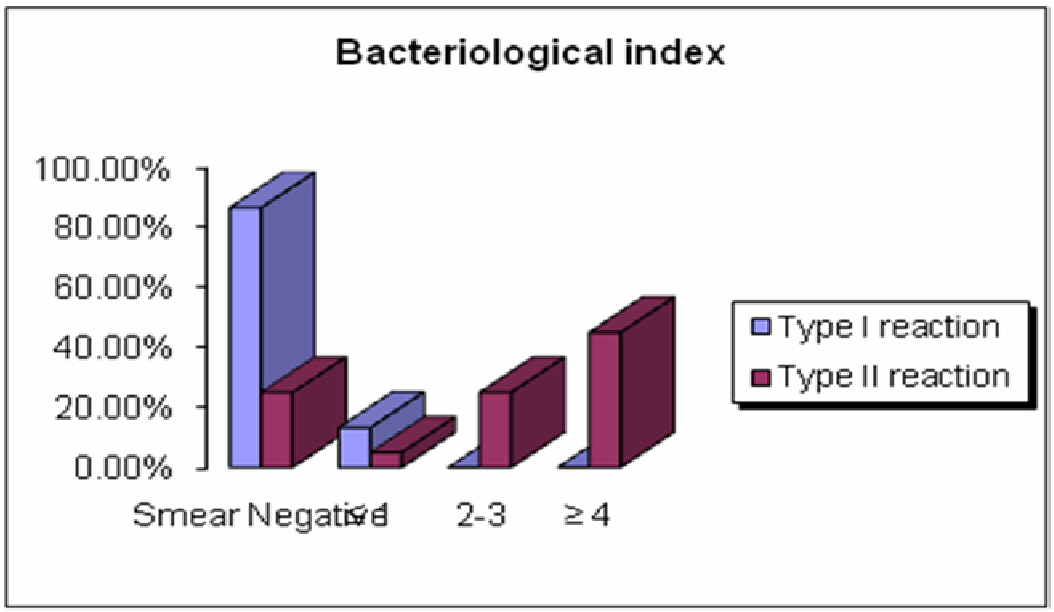


FIGURE 8

severe reaction and 4 (30.76%) had moderate reaction. 7 out of 13 patients (54%) had repeated episodes of flare ups and required steroids for more than 6 months. Among the patients with Type II reaction, 15 (75%) had exacerbation of reaction. Among these 15 patients, 10 (66.66%) of them had exacerbations in the standard 12 week period even before tapering could be completed when the dose of steroids was being brought down to <20 mg. The remaining 5 patients (33.33%) had exacerbations after the standard 12 week period when the steroids were continued in a low dose (<=10 mg) or stopped. Among these 15 patients, 7 (46.66%) had severe reaction and 7 (46.66%) had moderate reaction. Twelve (80%) of the patients who exacerbated had repeated flare ups and required steroids for more than 6 months (Table 6, Figure 7). Only one patient with Type II reaction could not be followed till the end of the study due to his sudden demise in a road traffic accident.

Twenty seven (90%) patients in Type I reaction were negative for AFB in slit skin smears and the other 3 (10%) had a bacteriological index (BI) of 1+. Nine patients (45%) with ENL had a BI of >=4, 5 (25%) had a BI between 2-3, 1 (5%) had a BI of 1+ and 5 (25%) had negative smears. (Table 7, Figure 8)

Study of the histopathological sections of patients with Type I upgrading reaction revealed an epitheloid cell granuloma in all patients with reversal

1.

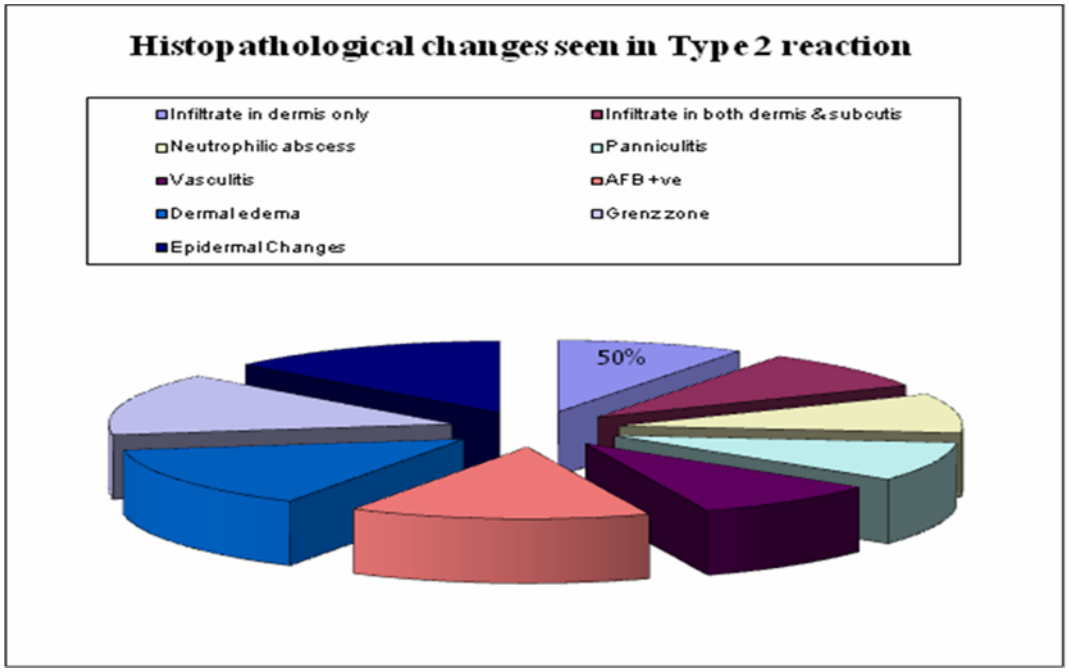


FIGURE 9

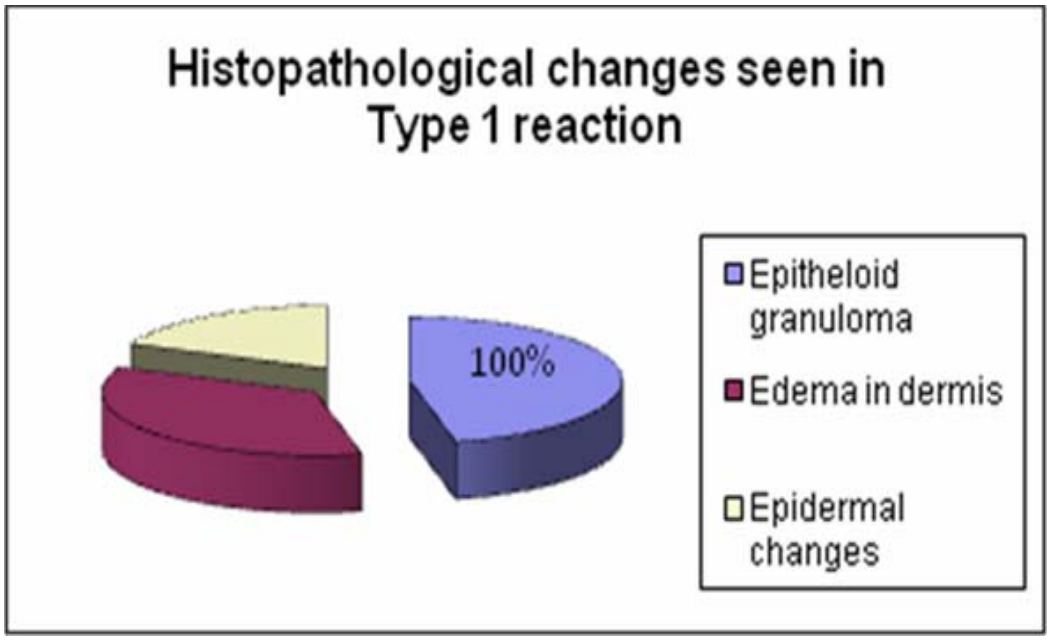


FIGURE 10

MULTIPLE ERYTHEMATOUS PATCHES OF TYPE I REACTION IN A PATIENT WITH BTHD

ERYTHEMATOUS PATCH OVER THE LEG IN A PATIENT WITH BTHD(TYPE I REACTION)

ERYTHEMATOUS PATCH OVER THE LEG IN A PATIENT WITH BTHD(TYPE I REACTION)

ERYTHEMATOUS PLAQUE OVER THE FACE IN A PATIENT WITH BTHD(TYPE I REACTION)

ERYTHEMATOUS PLAQUE OVER THE FACE IN A PATIENT WITH BTHD(TYPE I REACTION)

MULTIPLE ERYTHEMATOUS PLAQUES OVER THE BACK IN A PATIENT WITH BTHD(TYPE I REACTION)

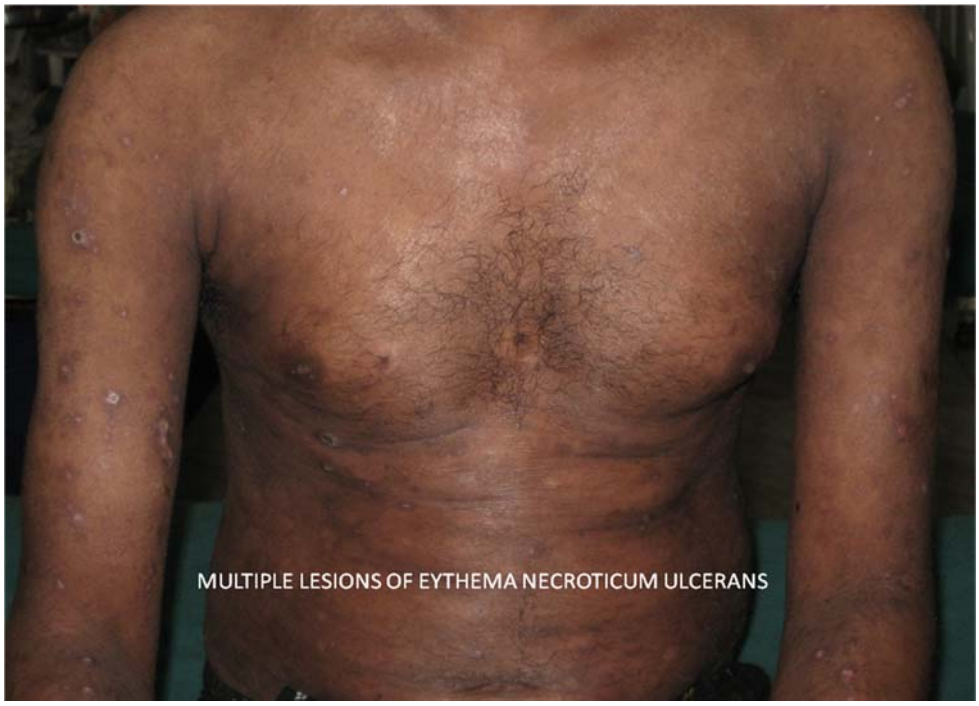
MULTIPLE ERYTHEMATOUS PLAQUES OF TYPE I REACTION IN A PATIENT WITH BBHD

ERYTHEMA NECROTICUM ULCERANS OVER THE EAR

MULTIPLE ERYTHEMATOUS NODULES IN A PATIENT WITH TYPE II REACTION

MULTIPLE NODULES OF ENL IN A PATIENT WITH HISTOID LEPROSY

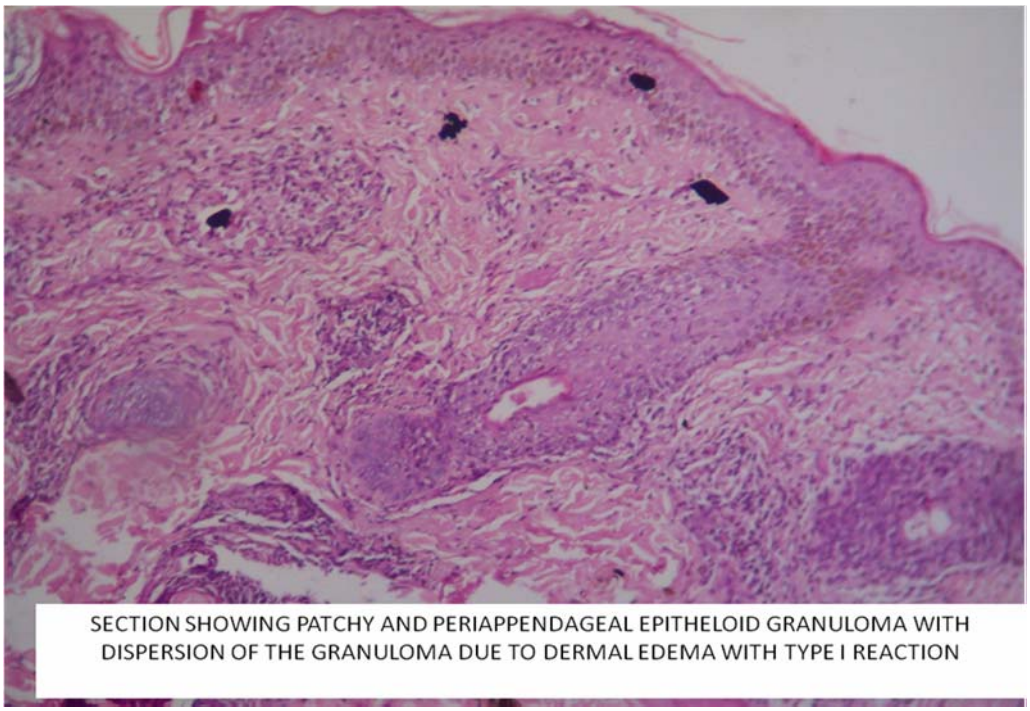
MULTIPLE NODULES OF ENL IN A PATIENT WITH HISTOID LEPROSY



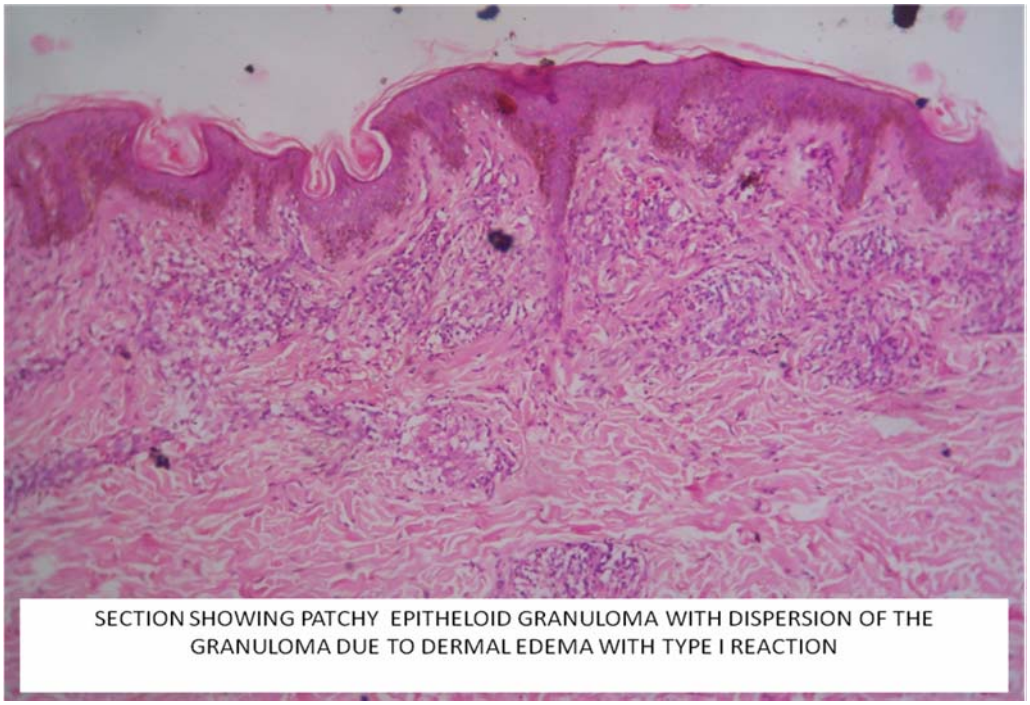
MULTIPLE LESIONS OF EYTHEMA NECROTICUM ULCERANS

MULTIPLE LESIONS OF ENL IN A PATIENT WITH LLHD

MULTIPLE LESIONS OF EYTHEMA NECROTICUM ULCERANS

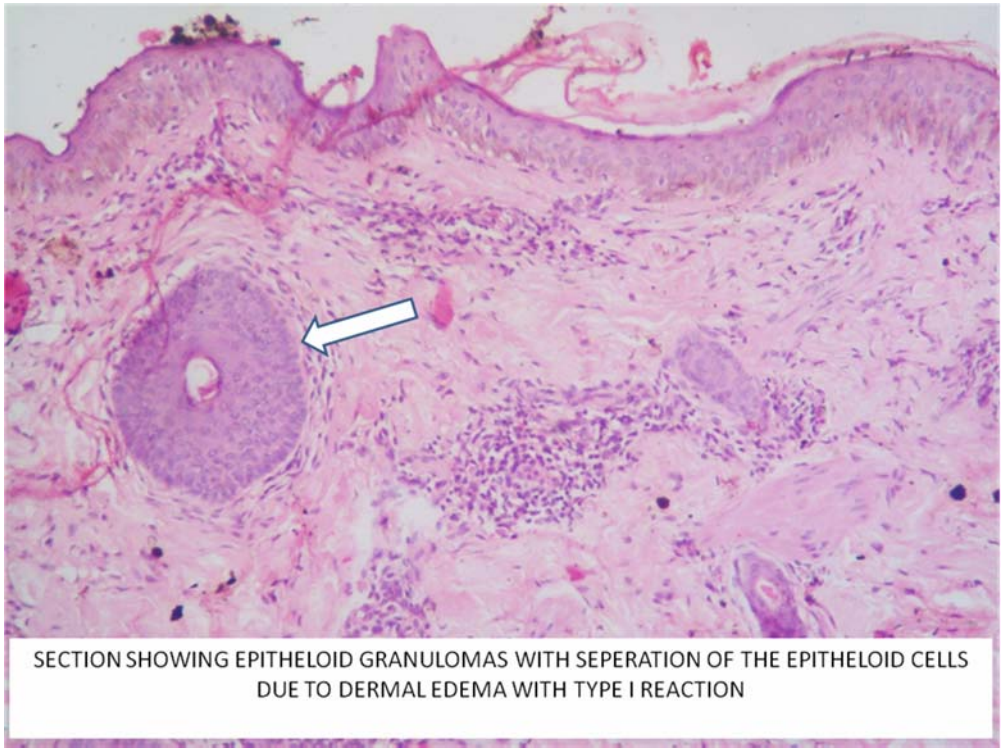


SECTION SHOWING PATCHY AND PERIAPPENDAGEAL EPITHELOID GRANULOMA WITH DISPERSION OF THE GRANULOMA DUE TO DERMAL EDEMA WITH TYPE I REACTION

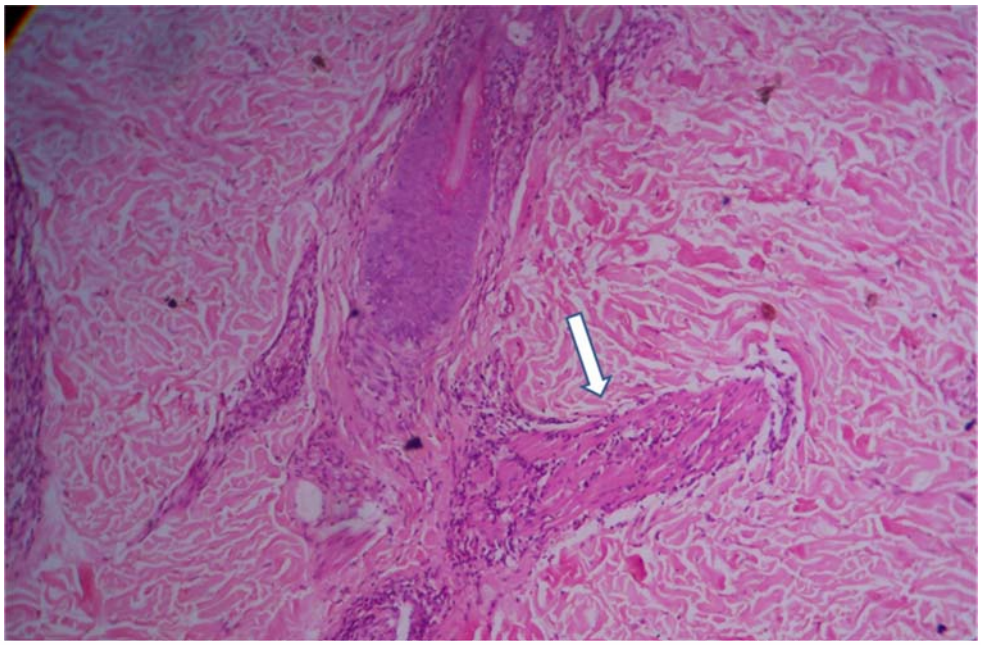


SECTION SHOWING PATCHY EPITHELOID GRANULOMA WITH DISPERSION OF THE GRANULOMA DUE TO DERMAL EDEMA WITH TYPE I REACTION

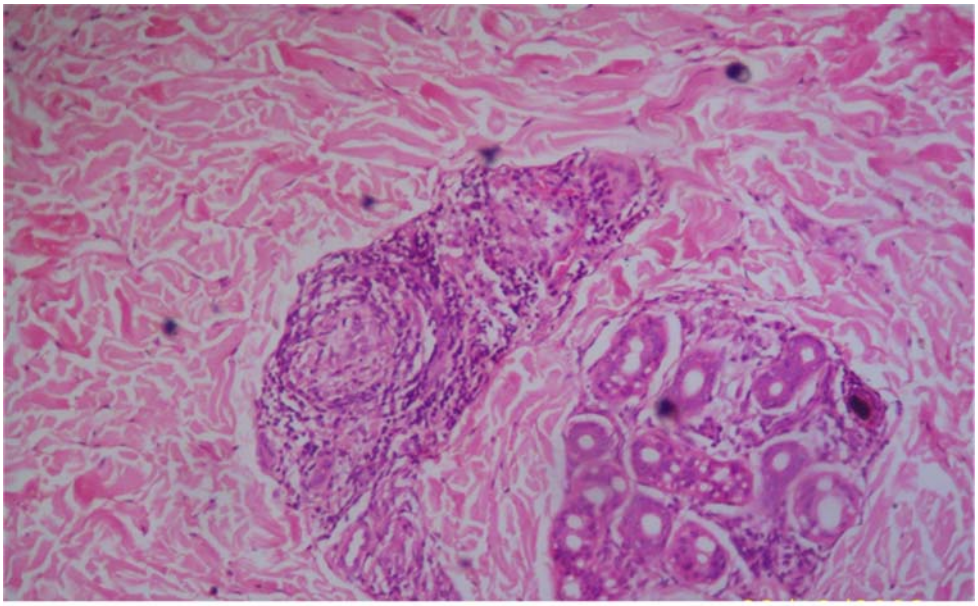
SECTION SHOWING DISPERSION OF EPITHELOID CELL GRANULOMA DUE TO DERMAL EDEMA WITH LANGERHANS GIANT CELL WITH TYPE I REACTION



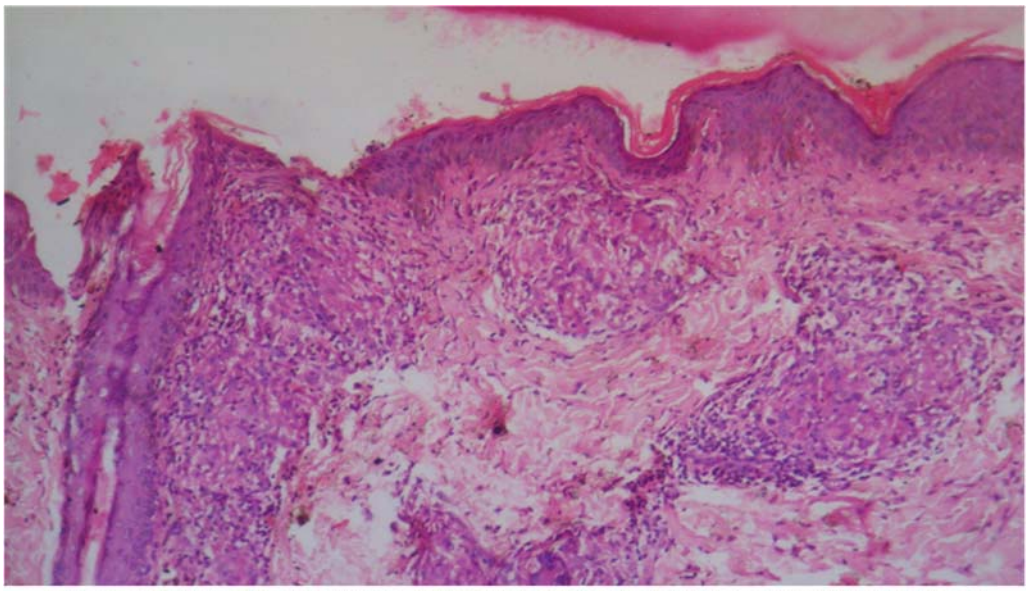
SECTION SHOWING EPITHELOID GRANULOMAS WITH SEPERATION OF THE EPITHELOID CELLS DUE TO DERMAL EDEMA WITH TYPE I REACTION



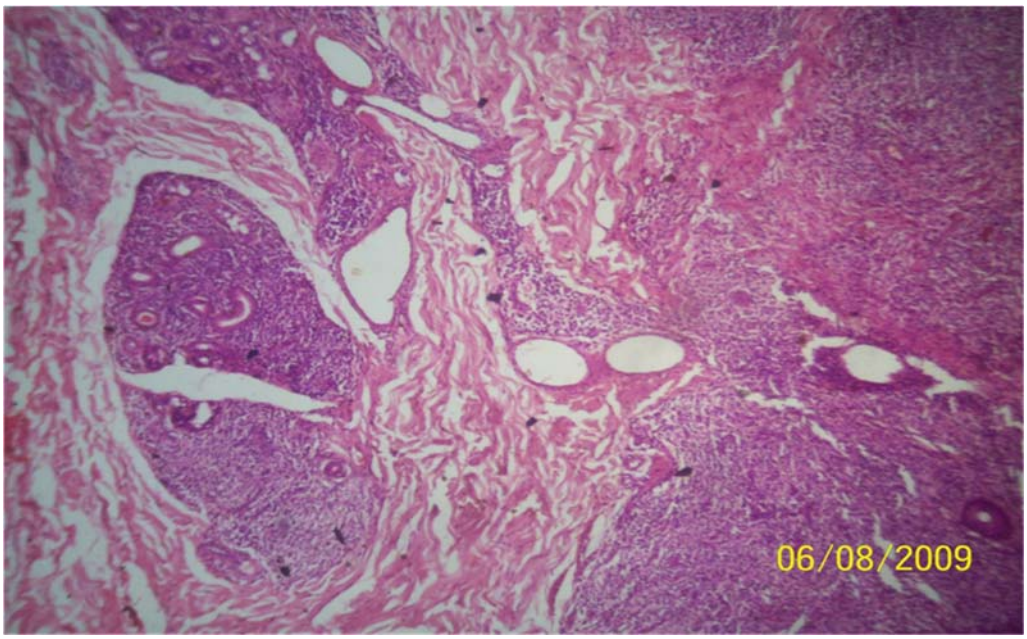
SECTION SHOWING DESTRUCTION OF THE ERECTOR PILI MUSCLE IN A PATIENT WITH TYPE I REACTION



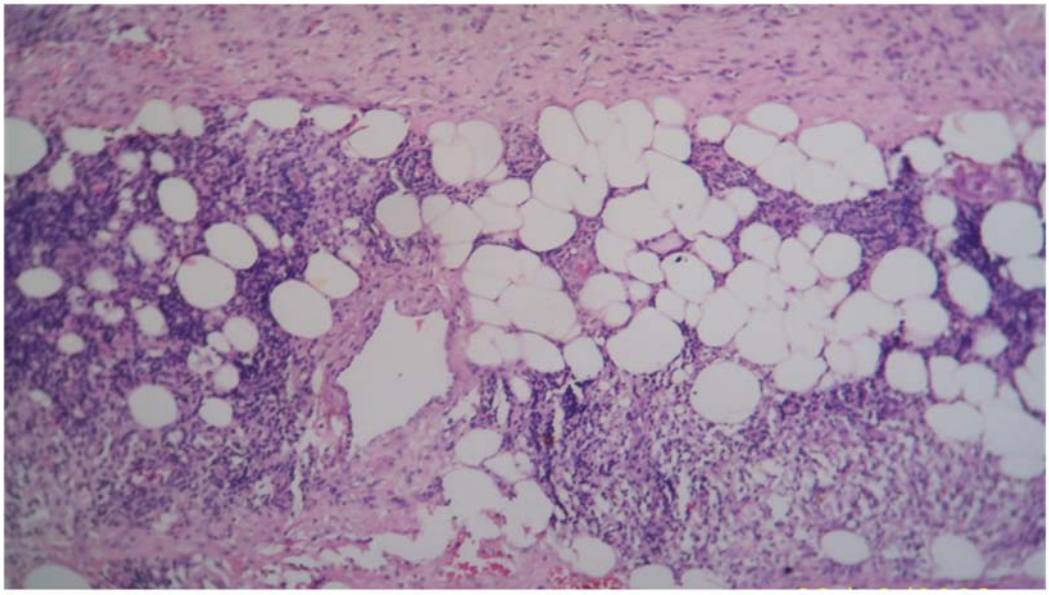
SECTION SHOWING INFLAMMATORY INFILTRATE AROUND NEUROVASCULAR BUNDLE AND SWEAT GLAND IN A PATIENT WITH TYPE I REACTION



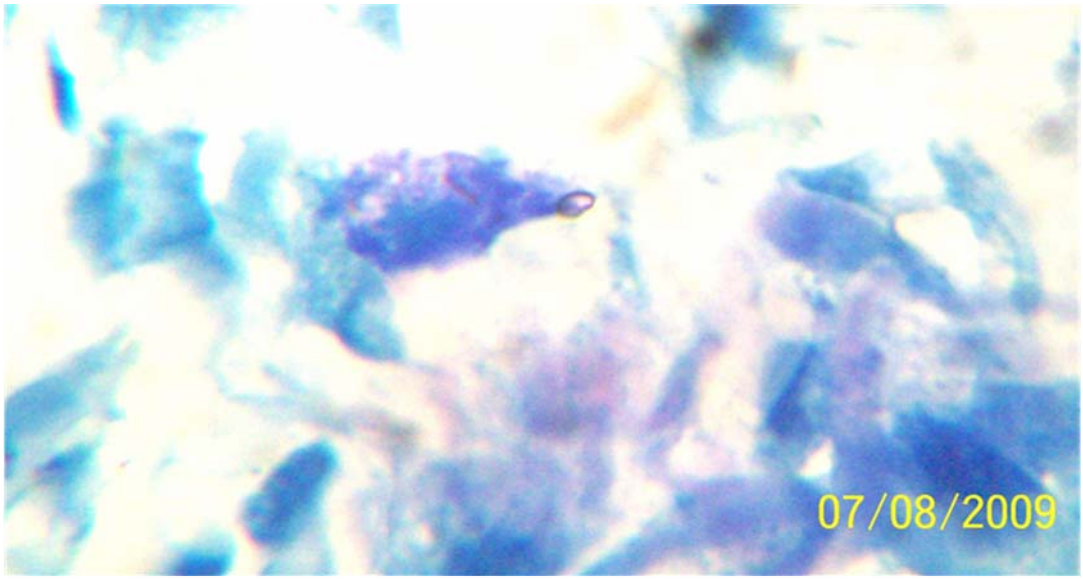
SECTION SHOWING DENSE PATCHY AND PERIAPPENDAGEAL INFLAMMATORY INFILTRATION WITH LANGERHANS GIANT CELLS IN A PATIENT WITH TYPE I REACTION



SECTION SHOWING DENSE NEUTROPHILIC INFILTRATION WITH VASCULITIS IN A PATIENT WITH TYPE II REACTION



SECTION SHOWING SEPTAL PANNICULITIS BENEATH A FOCUS OF MACROPHAGE INFILTRATES IN THE DERMIS IN A PATIENT WITH TYPE II REACTION



SECTION STAINED WITH FITE FORACO STAIN SHOWING A M.LEPRAE BACILLUS INSIDE A MACROPHAGE

reaction. An increase in the number of lymphocytes and multinucleate giant cells was also observed. Foci of fibrinoid necrosis and destruction of the appendages were seen in 21 (75%) patients. Edema in the dermis with hazy collagen fibers were seen in 21 (75%) of them. Epidermal changes were seen in 8 (40%) of the patients, with 5 of them having an epitheloid granuloma eroding into the epidermis. All these features correlated with the degree of severity of the clinical presentation. In patients with downgrading reaction, epitheloid granuloma admixed with lymphocytes and macrophages with acid fast bacilli were seen. In patients with Type II reaction, neutrophilic infiltration of the dermis overlying a focus of foamy macrophages was seen in all the patients. Dermal edema and Grenz zone were observed in 16 (80%) patients. Ten patients (50%) had neutrophilic abscess, panniculitis & vasculitis. Fragmented acid fast bacilli were seen in 16 patients (80%).(Table 8, Figure 9,10). Erythrocyte sedimentation rate (ESR) was found to be raised in all patients with Type II reaction. All other laboratory parameters were found to be within normal limits.

DISCUSSION

Several interesting observations have been made in our study. In our study, 50% of the patients were in the 21-40 year age group. The highest age incidence of both Type I and Type II lepra reactions have

been noted between 21-40 years (Hemerijckx F).[17] Male patients constituted 68% of the total which clearly correlates with the findings of the previous studies done at Belgian leprosy centre, Polambakkam, Madurantakam, South India[17]and Job et al[19].

92.85% of the patients in Type I reaction belonged to the borderline tuberculoid spectrum and 65% of the patients with Type II reaction belonged to the lepromatous spectrum in our study, which is also consistent with the findings of Kumar et al[31] and Vijayakumaran[106].

Among the patients with Type I reactions 40% developed the reaction before initiation of MDT. 10% developed Type I reaction within 6 months of starting MBMDT and 10% developed the reaction after 6 months. 23.33% of patients developed Type I reaction between 1-3 years after initiation of therapy and 13.33% developed the reaction between 3-5 years after starting therapy. 3.33% developed the reaction after 5 years of therapy. Kumar et al[31] reported that the incidence of reversal reaction was highest during 6-12 months after starting MDT. Vijayakumaran[106] et al had reported that most patients developed a reaction during the first 3 years of surveillance. This is different from that found in our study as 40% of our patients had developed Type I reaction de novo. Among the patients who developed Type II reaction, 30% each developed the reaction between 1-3 years and 3 -5 years after initiation of therapy respectively. Kumar et al[31] reported that ENL occurred mostly during 2nd

or 3rd year following MDT. This has correlated well with the findings in our study. In histoid leprosy, ENL reaction has been reported by some authors, [26,27,28,29.] . We had three patients with histoid leprosy who developed erythema nodosum leprosum (ENL). One of them developed ENL during the first year of treatment with MBMDT (multibacillary multidrug therapy) and two of them developed the reaction post MBMDT.

Apart from raised erythematous skin lesions, which were seen in all patients, neuritis was the predominant feature in Type I reaction, and was seen in 47% of the patients. Deformities like claw hand, foot drop and facial palsy was seen in 13%, 7% and 3% of the patients respectively in our study. Sharma[107] reported that 7.9% of patients developed claw hand during and after MDT. Richardus[108] also reported that 7.9% of previously normal MB patients developed nerve function impairment due to reaction. In our study, claw hand was seen in 13% and nerve function impairment in 20% (one patient had both claw hand and foot drop) which is only slightly higher than that seen by Sharma[107] and Richardus.[108] In patients with type II reaction, fever was noted in all the cases, arthralgia in 70%, edema of extremities in 85% and neuritis in 40% of the cases. All these findings of our study correlate well with those of Kumar et al[31].

Exacerbation of Type I reaction was seen in 43% of the cases with most of them (77%) developing it after 12 weeks of steroid therapy. All

those patients who had severe reaction required steroids for more than 6 months. In case of Type II reaction, exacerbations were observed in 75% of the patients with 50% of them observing exacerbations within 12 weeks of steroid therapy when the dose was being tapered to <20 mg. All those patients who had severe reaction required steroids for more than 6 months. Shen et al[109] found that the standard 12 week regime of prednisolone was effective only for mild Type I and Type II reaction cases. This regime was not effective for severe cases of reactions especially Type II reactions. This correlated with the finding of our study.

The histopathological features correlated well with the clinical findings. The clinical presentation of erythematous, tender plaques of Type I reaction correlated histologicaly with epitheloid granuloma extending up to the epidermis and dermal edema in 75% of the patients. An increase in the number of lymphocytes and multinucleate giant cells was also observed. This has also been reported by Ridley DS and Radia KB[108]. Foci of fibrinoid necrosis and destruction of the appendages were also seen in 75% of patients. This observation has also been made by Ridley DS[109]. Epidermal changes were seen in 40% of the patients, with 62.5% of them having an epitheloid granuloma eroding into the epidermis. This correlated clinically in those patients with severe form of reaction with erythematous plaque and pain over the lesions. Edema in the dermis with hazy collagen fibers were seen only in 75% of the cases which probably may be because of use of steroids in these patients prior to biopsy. In patients with downgrading reaction, lymphocytes admixed with macrophages were seen. Ridley and Radia[108] have reported increased numbers of macrophages and bacilli in histopathology sections

of patients with downgrading reaction. This is similar to the findings of our study. In patients with Type II reaction, all patients had neutrophilic infiltration of the dermis overlying foci of foamy macrophages. Dermal edema and grenz zone were observed in 80% of the cases. In most of the patients, neutrophilic abscesses, panniculitis and vasculitis were observed. As reported by Vinod Kumar Sharma[110] polymorphonuclear invasion of the vessel wall is a characteristic finding[110]in ENL. Our study has confirmed this finding.

Some other interesting findings were noted in our study. One patient was initially diagnosed as a case of BB down grading to BL Hansen's disease. He later developed ENL and required systemic steroids for a period of one year. After a year of quiescence, he developed late reversal reaction. One patient who was diagnosed with histoid Hansen's disease subsequently developed ENL about 3 years after initiation of MDT. We had another patient with Histoid Hansen's disease, who also went on to develop ENL 3 months after initiation of MDT. One patient presented with ENL as the first manifestation of leprosy.

CONCLUSION

1. The majority of the patients seen in either reaction were in the 21-40 years age group which corresponds to the highest age incidence of both Type I and Type II lepra reactions noted in other studies. There was an increased incidence of reactions in male patients constituting 68% of

the total number of cases. The sex ratio observed was 2.1**.** This high incidence in males could probably be due to increased tendency of males to seek prompt medical attention. The mean age of patients with Type I reaction was 39.8 years and the sex ratio 1.3. The mean age of patients with Type II reaction was 37.5 years and the sex ratio 4.0. The high incidence of Type I and Type II reactions in 21 -40 years reflects the high incidence of leprosy in this age group.

2. Most of the patients with Type I reaction had borderline tuberculoid leprosy. Even though most of the patients who developed type II reaction were primarily diagnosed with lepromatous leprosy, there were three patients with histoid leprosy who went in for ENL. An increasing trend of patients with histoid leprosy developing ENL has been found in this study. Studying a larger sample size may further confirm this finding. Type III reaction was not seen in any of the patients.

3. Among the patients with Type I reaction, a great proportion of them developed the reaction de novo, next to which most of them developed the reaction 1-3 years after initiation of MDT. Most of the patients with Type II reaction (60%) presented between 1 -5 years following diagnosis and treatment. A tendency for ENL to present de novo has also been found in this study. Type I reaction occurring de novo is a cause for concern as this can result in neuritis and deformity. Two patients presented with ENL de novo (one lepromatous and the other

borderline lepromatous). This calls for need to improve the surveillance for early detection and prompt treatment of the disease as it affects both the individual and the society in spread of the disease.

4. Neuritis (predominantly ulnar neuritis) was the predominant feature in addition to raised erythematous skin lesions in Type I reaction. Newer deformities occurring during the reactional episodes were seen in 20% of the cases, which is quite significant. This increased incidence of neuritis demands early intervention and prompt treatment to avoid deformities and improvement in the quality of life of the patients . In patients with Type II reaction, fever, arthralgia, edema of extremities, neuritis and lymphadenitis were the predominant features noted. Iritis and orchitis were seen in patients with severe Type II reaction. So it is imperative to look for these findings in patients to initiate early treatment and prevent catastrophic consequences. Patients with moderate and severe Type I and Type II reaction were found to require steroids for prolonged periods.

5. The clinical features of patients with both Type I and Type II reactions correlated well with the histopathological findings. The clinical severity of Type I reaction correlated histopathologically with the degree of dermal edema. Patients with severe ENL reaction were found to have neutrophilic infiltrates, neutrophilic abscess, panniculitis and vasculitis on histopathological examination.

REFERENCES

2. Wade H.W. Int. J. leprosy 23 (1955): 370

3. Tajiri. Int. J. Leprosy 1955: (370)

4. Murata. M. Japanische Zeit Schrift fur Dermatologie Urologie 12 (1912): 1013-1051

5. De Souza Lima & Maurano. Rev Brasileina Leprol. 7 (1939): 173-174 (Spl. issue)

6. Pecarano. Rev Brasileina Leprol. 10 (1942): 67-83

7. Pogge and Ross. Int. J. Leprosy 14(1946): 49-54

8. Wolcott R. R. Int. J. Leprosy 15 (1947) : 380-388

9. Schujman S. Rev Argentina Dermatosif 31 (1947): 506-512

10. Roche et al. Int. J. Leprosy 19 (1951): 137-145

11. Contreras et al. Int. J. Leprosy 20 (1952): 707-711

12. Davison A.R. Leprosy Review 30 (1959): 112-113

13. Jopling W.H. Leprosy Review 30 (1959): 194-196

14. Latapi and Zamora. Int. J. Leprosy 16 (1948): 421-430

15. "Detection of IL-13, IL-10 and IL-6 in leprosy skin lesions of patients during prednisolone treatment for Type I reaction" – Sara E. Atkinson et al, International Journal of Leprosy Vol72 No.1 (2004)

16. Sharma P. Kar H.K., Misra R.S, Mukerjee A, Kaur H, Mukerjee R and Rani.R, Reactional states and neuritis in Multibacillary patients following MDT with or without immunotherapy with Mycobacterium w antileprosy vaccine. Leprosy Review 71(2000): 193-205.

17. Deepika Pandhi, Shilpa Mehta, Subhav Agarwal and Archana Singal – Erythema Nodosum Leprosum Necroticans in a child –an unusual manifestation. International Journal of Leprosy Vol.73 No.2, 2005.

18. Report on the activities and leprosy control campaign during 1955-58 of Belgian leprosy centre, Kolambakkam, Madurantakam, South India, Jewaker Press 1959.

19. Sehgal V.N, and Chaudhary. A "Leprosy in children: A prospective study" – International Journal of Dermatology 32 (1993): 194-197.

20. Job et al – International Journal of Leprosy 32 (1964) 177-183

21. Browne S.G.J. Chronic ds 16 (1963): 23 - 30

22. Guinto et al, J.Philippine Med.Association 38 (1962): 929-940.

23. Samuel L. Moschella in Dermatology, edited by Samuel L.Moschella 3rd edn. (1994)

24. Ridley. D.S. Leprosy Review. 53 (1982): 19-26.

25. W.H. Jopling in Hand book of Leprosy 5th edn,1996

Bryceson A.and Pfaltzgraf R.E in Leprosy edited by Robert C. Hastings (1985)

26. Waters MFR et al Int. Journal of leprosy 39 (1971) 417-428.

27. Price E.W. and Fritzherbert H, Int. J. Leprosy 34(1966): 367-374.

28. Suresh.K.Sharma, Namitha Rath, R.K.Gautham, P.K.Sharma, E.K.Jain, HK Kar Histoid Leprosy with ENL reaction, IJDVL

29. Kaur I, Dogra S, De D, Saikia U.N in Histoid Leprosy, a study of 40 cases from India. British Journal of Dermatology 160(2) : 305-310 (Feb-2009).

30. Mahapatra S.B., Ramu.G – Leprosy in India 45 (1976)

31. Kumar B, Dogra S, Kaur.I, Epidemiological characteristics of Leprosy reactions :15 years experiences from North India. Int.J. Leprosy and other mycobacterial disease 2004;72:125-133.

32. Rea T.H and Levan N.E Archives of Dermatology 111(1975)

33. V.N. Sehgal in Clinical leprosy (1979)

34. Jopling W.H. in Hand book of Leprosy 5th edition (1996)

35. Barnes E.W et al, Lancet – I (1974) : 898

36. Muir E. Leprosy review 33 (1962) : 240

37. Stein .A. International Journal of Leprosy 3 (1935): 137

38. Dharmendra – Notes on Leprosy Govt. of India, Ministry of Health II edn (1967) Pg. 54

39. Tei Chman G. in Leprosy Review 20 (1949) 89-94

40. Pankaj Sharma, Kar H.K, Misra R.S, Ashok Mukherjee, Harvinder Kaur, Rama Mukherjee and Rajni Rani. Reactional states and neuritis in multibacillary patients following MDT with/ without immunotherapy with Mycobacterium w anti leprosy vaccine. Leprosy Review No.2 Vol.71

41. Sunil Dogra, Inderjeet Kaur, Bhushan Kumar. Phimosis as a presenting manifestation of Genital involvement in Leprosy. International Journal of Leprosy, Vol.72, No.1 (2004)

42. Ritika Gupta, Archana Singal & Deepika Pandhi. Genital involvement and Type I reaction in childhood leprosy. Leprosy Review 76, 253-257 (2005)

43. Tarun Narang, Sunil Dogra and Inderjeet Kaur . Borderline Tuberculoid Leprosy with Type I reaction in an HIV patient – A phenomenon of immune reconstitution. International Journal of Leprosy Vol.73, No.3 (2005)

44. Feuth M, Wim Brandsma J, Faber W.R, Bhattarai. B, Feuth.T, Anderson. A.M. Erythema nososum leprosum in Nepal : a retrospective study of clinical features and response to treatment with prednisolone or thalidomide. Leprosy Review 79, 254-269 (2008)

45. Ramu. G and Dharmendra in Leprosy Vol.I (1978)

46. Petro T.S. Bullous type of reaction mimicking pemphigus in lepromatous leprosy. Ind. J. Leprosy 1996; 68: 179-181.

47. Rijal A, Agarwal S, Agarwal A, Lakney M. Bullous erythema nodosum leprosum- a case report from Nepal. Leprosy Review (2004) 75, 177-180.

48. Nand Lal Sharma, Vikram.K.Mahajan, Vikas. C. Sharma, Sandip Sarin and Ramesh Chander Sharma. Erythema nodosum leprosum and HIV infection – A therapeutic experience – Int. J. of Leprosy Vol.73 No.3 (2005)

49. Gebre S, Saunderson P, Messele T and Byass P. The effect of HIV status on the clinical picture of Leprosy" a prospective study in Ethiopia. Leprosy Review 71 (2000) 338-343.

50. Patki A.H. Some possible interactions of M.leprae and HIV in peripheral nerves. Int. J. Lepr other Mycobact Dis. 59(1991) 331-332

51. Bwire. R and Kawuma. H.J.S. Type I reactions in leprosy, neuritis and steroid therapy : the impact of the human immuno deficiency virus. Trans. R. Soc. Trop. Med. Hyg. 88 (1994) 315-316.

52. Vreeburg A.E.M. (Clinical observations on Leprosy patients with HIV-1 infection in Zambia Lep. Rev. 63 (1992) 134-140.

53. Karat et al. British Medical Journal IV (1968) 223-224.

54. Upreet Dhaliwal, Sandeep Mohanty and Sambit. N. Bhattacharya . Erythema Nodosum Leprosum and orbital involvement. International Journal Leprosy Vol.71, No.1 (2003)

55. Bhattacharya et al. Leprosy Review 44 (1973) 29-32.

56. Datz F.L. Clinical Nucl. Medicine : 12 (1987) 212 – 214.

57. Rea T.H.and Levan N.E. Archives of Dermatology 114(1978) 1023-1028.

58. Dr. Rea T.H. Reversal reaction occurring 16 years after beginning antibacterial treatment – Leprosy Review March 2004.

59. Dr.Opromolla D.V.A. Some considerations in the origin of Type I reactions in Leprosy. Int. Journal of Leprosy Vol. 73 No.1 2005

60. Wade H.W. Tuberculoid changes in Leprosy II Lepra reaction in tuberculoid Leprosy. International Journal of Leprosy Dis 2(2) 1934: 279-292.

61. Wade H.W, Rodriguez J.N & Tolentino.J. The course of open cases of tuberculoid Leprosy at Ceber Leprosarium. International Journal of Leprosy Dis 7 (4). 1939: 473 – 494.

62. Shetty V.P., Wakade A and Antia N.H.A. A high incidence of viable M.leprae in post MDT & recurrent lesions in tuberculoid pts. Leprosy Review 72 (3), 2001: 337 – 344.

63. IADVL Text book of Dermatology 3rd edn(2008) edited by R.G. Valia and Ameet R.Valia published by Bhalani publishing House, Mumbai.

64. Leprosy edited by Robert C. Hastings and Opromolla D.V.A (1994)

65. Little.D, Khanolkar-Young.S, Coulthart.A, Suneetha.S, Lockwood.D. Immunohistochemical analysis of cellular infiltrate and gamma interferon, IL-12 and inducible NO synthase expression in leprosy Type I reactions before and during prednisolone treatment. Clin. Exp. Immunology 69 (2001): 3413 – 3417.

66. Atkinson et al. Detection of Il-13, IL-10, IL-6 in leprosy skin lesions of patients during prednisolone treatment for Type I reactions. Int. Journal of Leprosy vol72 No.1 2004.

67. Cooper et al. IFN- α and NO is mycobacterial disease : new jobs for old hands. Trends Microbiol. IO (2002): 221 - 226.

68. Khanolkar – Young et al. TNF – α synthesis is associated with skin and peripheral nerve pathology of Leprosy reversal reactions. Clin. Exp Immunology 99 (1995): 196-202.

69. Faber et al. Serial measurement of serum cytokines cytokine receptors and neopterin in leprosy patients with reversal reactions. Leprosy Review 75(3), 2004: 274-281.

70. Dharmendra & Desikan K.V. in "A Manual of Leprosy" edited by R.H. Thangaraj III edn. (1983) Pg. 20.

71. Wemambu SNL et al Lancet ; 1, (1969) 933 – 935.

72. Chugh et al. Post graduate Med. Journal 59 (1983)

73. Patnaik et al. Int. Journal of Leprosy 57 : (1989) 499-505

74. Mshana et al. Leprosy Review 53 (1982)

75. Belchu et al. Int. Journal of Leprosy 50 (1982) Pg.36

76. Modlin et al. Int. Journal of Leprosy 50 (1982) Pg.36

77. Ajith et al. Study of Apoptosis in skin lesions of Leprosy in relation to treatment and Lepra reactions. Int. Journal of Leprosy vol73, No.4, 2005.

78. Hockenbery D. Defining Apoptosis. Am.J.Pathology 146 (1995): 16-19.

79. Oliveira R.B et al. Neutrophils isolated from leprosy patients release TNF – α and exhibit accelerated apoptosis in vitro. J. Leukoc. Biol. 65 (1999): 364 – 371.

80. Donald M. Pillsbury et al in Dermatology (1956) W.B.Saunders 173-174.

81. Ben Naafs. Treatment duration of reversal reaction : a reappraisal Back to the past. Leprosy Review (2003) 74, 328-336

82. Sheskin. J. Thalidomide in the Treatment of Lepra Reactions, Clin.pharmacol. Ther., 1965; 6 : 303-306.

83. Wnendt.S Zwingenberger. K. Thalidomide Chirality, Nature : 1997; 385 : 303-304.

84. Franks ME, Macpherson GR, Figg W.D. Thalidomide. Lancet 2004, 363 : 1802-1811.

85. Giridhar BK. Immuno pharmacology of drugs used in Leprosy reactions, IJDVL. (1990) : Vol.56 Issue 5 : 354 – 363.

86. Sarojini. P.A. and Mshara R.N. Leprosy Review 54 (1983) 151.

87. Mathur NK. Bumb RA and Mangal HN: Oral zinc in erythema nodosum leprosum, Indian J Lepr, 1983; 55: 547-552.Kaushar K.Verma, P.Srivastava, Anil Minz and Kamna Verma. Role of azathioprine in preventing recurrences in patient of recurrent erythema nodoum leprosum. Leprosy Review (2006)77, 225-229.S.P.K Athreya. Azathioprine in controlling Type II reactions in leprosy : a case report. Leprosy Review (2007) 78 : 290-292.

88. Langagergaard V, Pederson.L, Gislum M, Norgard.B. SorensenH.T. Birth outcome in women treated with azathioprine or mercaptopurine during pregnancy : A Danish nationwide cohort study. Aliment Pharmacol Ther., 2007; 25 : 73-81.

89. Steven.L. Walker, Michael F.R, Waters & Diana N.J. Lockwood. The role of thalidomide in the management of erythema nodosum leprosum. Leprosy Review (2006)77, 225-229.

90. Kalyan Banerjee, Raghubir Banerjee. Management of erythema nodosum leprosum by Mycophenolate Mofetil (2008) Vol.53 Issue:3 Pg.142-143.

91. PC Singh, S.Mishra, M.Mishra. Pentoxyphylline in reactions in leprosy (1996) Vol : 62, Issue : 3 Pg.163-164.

92. Kar HK, Roy R.G. Comparision of colchicine and aspirin in the treatment of Type II lepra reaction. Leprosy Review (1988); 59 : 201-203.

93. Vides EA, Cabrera A, Ahern KP, Levis WR. Effect of Zafirlukast on Leprosy reactions. Int. J. Lepr. Other mycobact DTS, (1999) 67 : 71-75.

94. Faber W.R, Jensema AJ, Goldschmidt EWF. Treatment of recurrent erythema nodosum leprosum with infliximab. N.Engl. J. Med., 2006 ; 355 : 739.

95. WHO expert committee on leprosy. Technical report series: 874, 1998.

96. Hot topics in leprosy – Lepr. Rev. (2003) 7487-88 Sanjcer Handa & Sunil Dogra.

97. Li Huan Ying. Analysis of reversal reaction in leprosy patients following fixed duration MDT. Paper at the Asian leprosy Congress, Agra 2000.

98. Little D, Khanolkar-Young S, Coulthart A, Suneetha S, Lockweed D, Immunohistochemical analysis of cellular infiltrate and gamma interferon, interleukin and inducible Nitric oxide synthase expression in

leprosy type I (reversal) reactions before and during prednisolone treatment. Infect Immun, 2001 ; 69 : 3413-3417.

99. Stephen L. Walker and Diana N.J. Lockweed. Leprosy Type I reactions and their management. Leprosy Review (2008) 79, 372-386.

100. Thangaraj E.S. in A manual of Leprosy edited by R.H. Thangaraj 6th edn. (1989).

101. Expert WHO committee on Leprosy World Health Organ Tech Rep. Ser., 1998; 874 : 1-43.

102. http://www.ilep.org.uk/content/documentholder.hem?tb09eng.pdf.

103. Vikram .K. Mahajan, Sharma N.L, Sharma R.C and Ashok Sharma. Pulse Dexamethasone, oral steroids and Azathioprine in the management of Erythema Nodosum Leprosum. Leprosy Review (2003) 74, 171 – 174

104. Vijayakumaran P, Manimozhi N, Jesudasan K. Incidence of late lepra reaction among multibacillary leprosy patients after MDT. Int J Lepr other Mycobact Dis, 1995; 63: 18 – 22

105. Sharm P, Kar HK, Beena KR et al. Disabilities in multibacillary leprosy patients: before, during and after multidrug therapy. Indian J Lepr, 1996; 68:127 – 136

106. Richardus JH, Finlay KM, Croft RP et al. Nerve function impairment in leprosy at diagnosis and at completion of MDT: a

retrospective cohort study of 786 patients in Bangladesh. Lepr Rev, 1996; 67: 297 – 305

107. Jiaping Shen, Musang Liu, Min Zhou and Li Wengzhong. Occurrence and management of leprosy reaction in China in 2005. Lepr Rev, 2009; 80: 164 -169

108. Ridley DS and Radia KB. The histological course of reactions in borderline leprosy and their outcome. Int. J. Lepr. 1981; 49: 383 – 392.

109. Ridley DS. Skin biopsy in leprosy, 2nd edition. Switzerland: documenta Geigy; 1985 pg 26

110. IADVL textbook of Dermatology 3rd edition, edited by R.G.Valia and Ameet R. Valia, Bhalani publishing house, Mumbai.

MASTER CHART

NAME	AGE	SEX	DIAGNOSIS	Duration of ds before reaction onset	Fever <100° F	Arth	OH	OF	LTM	Epi	Orch	Iri	Neu	CH	FD	FP	UL	Clinical Grading of reaction	Exacer in 12	after 12	Rptd Exacer	BI	Epi changes	GZ	Dermal Edema	Inf in dermis	Inf D+S	NA	Panni	Vascu	AFB +ve (Frag
arthasarathy	40	M	BLHD/ENL	Started with R	+	-	-	-	-	+	-	-	-	-	-	-	-	mod	√		+	3+	+	-	+	+	-	-	-	+	+
Shravan	23	M	LLHD/ENL	Started with R	+ >102° F	+	+	+	+	+	-	-	+	-	-	-	-	severe	√		+	3+	+	+	+	-	+	+	+	+	+
Prakash	25	M	LLHD/ENL	3yrs	<102° F	-	+	+	-	-	-	-	-	-	-	-	-	mod	√		-	- ve	+	+	+	-	+	+	+	+	+
hagwan Das	62	M	HHD/ENL	3-5yrs	<100° F	+	-	-	-	-	-	-	-	-	-	-	-	mod	√		+	5+	-	-	-	+	-	-	-	-	+
athavarayan	55	M	LLHD/ENL	4 months	>102° F	+	+	+	+	+	+	-	-	-	-	-	-	severe	√		+	4+	+	+	+	+	-	+	-	-	+
Selvam	15	M	HHD/ENL	3 months	100-102°F	-	+	+	+	-	-	-	-	-	-	-	-	mod	√		+	5+	-	-	-	+	-	-	-	-	-
Mani	37	M	LLHD/ENL	1-3yrs	100-102°F	+	+	-	-	-	-	-	+	-	-	-	+	severe	√		+	4+	+	-	+	-	+	+	+	+	+
Venkatesh	38	M	LLHD/ENL	3-5yrs	100-102°F	-	+	-	-	+	-	-	-	-	-	-	-	mod	√		+	- ve	-	+	-	+	-	-	-	-	-
Kadirvel	60	M	Relapse LLHD/ENL	1-3yrs	100-102°F	-	+	+	-	+	-	-	-	-	-	-	-	mod	–		-	5+	-	+	+	+	-	-	-	-	-
Parthiban	25	M	Old LLHD/ENL	3-5yrs	>102° F	+	+	+	-	-	-	-	+	+	-	-	-	severe	√		+	1+	+	+	+	-	+	+	+	+	+
Chelladurai	51	M	Old BLHD/ENL	1-3yrs	<100° F	+	+	-	+	+	-	-	-	-	-	-	-	mod	–	√	+	- ve	+	+	+	-	+	+	+	+	+
Padmanaban	35	M	Relapse LLHD/ENL	1-3yrs	>102° F	+	+	+	+	-	-	+	+	-	-	-	+	severe	√		+	5+	+	+	+	-	+	+	+	+	+
Deenadayalan	45	M	Old BLHD/ENL	3-5yrs	<100° F	-	-	-	-	-	-	-	-	-	-	-	-	mod	–		-	- ve	+	+	+	+	-	+	-	-	+
Rajendran	40	M	Old LLHD/ENL	3-5yrs	<100° F	+	+	-	+	-	-	-	-	-	-	-	-	mod	–		-	4+	+	+	-	-	+	-	+	-	+
Yagesh	27	M	Old LLHD/ENL	3-5yrs	100-102°F	+	+	-	+	+	+	-	+	+	-	+	-	mod		√	-	3+	+	+	+	-	+	+	+	+	+
Venkatesh	24	M	Old LLHD/ENL	>5yrs	100-102°F	+	+	-	-	+	-	-	-	-	-	-	-	mod		-	-	2+	+	+	+	+	-	-	-	-	-
Suseela	40	F	Relapse LLHD/ENL	4 months	100-102°F	+	+	-	-	-	-	-	+	-	-	-	-	mod		√	+	5+	+	+	+	-	+	-	+	-	+
eyalakshmi	35	F	Old HHD/ENL	5yrs	100-102°F	+	+	-	-	+	-	-	+	-	-	-	-	mod		-	-	- ve	-	+	+	-	+	+	+	+	+
Devi	42	F	Old LLHD/ENL	1-3yrs	100-102°F	+	+	-	-	-	-	-	+	-	-	-	-	severe		√	+	5+	+	+	+	+	-	-	-	+	+
Kumari	40	F	Old LLHD/ENL	5 months	>102° F	+	+	-	+	+	-	-	-	-	-	-	-	severe		√	-	2+	+	+	+	+	-	-	-	-	+

Gurumoorthy	29	M	BTHD/ TYPE I	Started with R	-	-	+	-	-	-	-	-	+	+	-	-	-	severe		√	-	- Ve	+	-	+	Epitheloid granuloma		-
Sunitha	30	F	BTHD/ TYPE I	Started with R	-	-	+	-	-	-	-	-	+	+	-	-	-	severe	-	–	-	- Ve	+	-	+	Epitheloid granuloma		-
Rani	40	F	BLHD/ TYPE I	1-3yrs	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	√		+	- Ve	-	-	-	Epitheloid granuloma		-
Rukmani	55	F	BTHD/ TYPE I	2 months	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	-		-	- Ve	-	-	+	Epitheloid granuloma		-
Deivanai	45	F	BB-BLHD/ TYPE I	Started with R	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	-	–	-	1+	+		-	Epitheloid granuloma + macrophages		-
Sumathy	15	F	Old BTHD/ TYPE I	3-5yrs	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	-	–	-	- Ve	-	-	-	Epitheloid granuloma		-
Senjurammal	60	F	Old BTHD/ TYPE I	3-5yrs	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	-	–	-	- Ve	+		+	Epitheloid granuloma		
Sunitha	32	F	BTHD/ TYPE I	8 months	-	-	+	-	-	-	-	-	+	-	-	-	-	severe	-	–	-	- Ve	+		+	Epitheloid granuloma		
Shanthi	30	F	BTHD/ TYPE I	1-3yrs	+	-	-	+	-	-	-	-	+	-	-	-	-	severe	-	√	+	- Ve	-	-	-	Epitheloid granuloma		-
Saradha	54	F	BTHD/ TYPE I	2-5yrs	+	-	+	-	-	-	-	-	+	-	-	-	-	mod	√		+	- Ve	+		+	Epitheloid granuloma		-
Yadhambal	45	F	Old BTHD/ TYPE I	3-5yrs	-	-	+	-	-	-	-	-	+	-	-	-	-	severe	√		-	- Ve	+		+	Epitheloid granuloma		-
Muniammal	61	F	BTHD/ TYPE I	11 months	-	-	-	-	-	-	-	-	+	-	-	-	-	mod		√	-	- Ve	-		+	Epitheloid granuloma		-

Karpagam	49	F	BTHD/ TYPE I	Started with R	+	-	-	+	-	-	-	-	+	-	-	-	-	severe	√		-	- Ve	-	-	+	Epitheloid granuloma				-
Vijaya	35	F	BTHD/ TYPE I	1 month	-	-	-	-	-	-	-	-	-	-	-	-	-	mod		√	-	- Ve	+		+	Epitheloid granuloma				-
Arun	18	M	BTHD/ TYPE I	Started with R	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	-	-	-	- Ve	-		+	Epitheloid granuloma				-
Pasupathy	51	M	Old BTHD/ TYPE I	1-3yrs	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	-	-	-	- Ve	+		+	Epitheloid granuloma				-
Tejuddin	60	M	Relapse BTHD/ TYPE I	5 months	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	-	-	-	- Ve	-		+	Epitheloid granuloma				-
Murugesan	30	M	BLHD / TYPE I	Started with R	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	-	-	-	1+	-		+	Epitheloid granuloma				-
Nagiah	55	M	BTHD/ TYPE I	Started with R	-	-	-	-	-	-	-	-	-	-	-	-	-	mod	-	-	-	1+	-		+	Epitheloid granuloma				-
Vijay	16	M	BTHD/ TYPE I	Started with R	+	-	+	-	-	-	-	-	+	+	+	–	-	severe	-	-	-	- Ve	-	-	+	Epitheloid granuloma				-
Velusamy	62	M	Old BTHD/ TYPE I	1-3yrs	-	-	-	-	-	-	-	-	-	-	-	-	-	mod		-	-	- Ve	-	-	-	Epitheloid granuloma				-
Adamshariff	24	M	BTHD/ TYPE I	>5yrs	-	-	-	-	-	-	-	-	-	-	-	-	-	mod		-	-	- Ve	-	-	+	Epitheloid granuloma				-
Pethi	43	M	Old BTHD/ TYPE I	1-3yrs	-	-	-		-	-	-	-	-	-	-	-	-	mod	-	-	-	- Ve	-	-	+	Epitheloid granuloma				-
Pintu	21	M	Old BTHD/ TYPE I	1-3yrs	+	-	+	-	-	-	-	-	+	+	-	-	-	severe	-	√	+	- Ve	+	-	+	Epitheloid granuloma				-
Gopal	45	M	BTHD/ TYPE I	Started with R	-	-	-	-	-	-	-	-	-	-	-	-	-	mod		-	-	- Ve	-	-	+	Epitheloid granuloma				-

Kumar	34	M	BTHD/ TYPE I	Started with R	-	-	-		-	-	-	-	-	-	-	-	-	mod	√	-	+	- Ve	-	-	+	Epitheloid granuloma					-
Karuppasamy	49	M	BTHD/ TYPE I	Started with R	-	+	-	-	-	-	-	-	+	+	-	-	-	severe		√	+	- Ve	+	-	+	Epitheloid granuloma					-
Devi prakash	26	M	BT-BBHD / TYPE I	Started with R	-	-	+	-	-	-	-	-	+	-	-	-	-	mod		-	-	- Ve	-	-	-	Epitheloid granuloma + macrophages					-
Velayudham	31	M	Old BTHD/ TYPE I	11 months	-	-	-		-	-	-	-	+	-	-	-	-	mod		√	+	- Ve	+	-	-	Epitheloid granuloma					-
Ganesan	32	M	BTHD/ TYPE I	1-3yrs	-	-	+	-	-	-	-	-	+	-	-	-	-	mod		√		- Ve	-	-	-	Epitheloid granuloma					-

KEY TO MASTER CHART

Oedema of hands - OH

Oedema of feet - OF

Lymphadenitis - Lym

Epistaxis - Epi

Orchitis - Orch

Iritis - Iri

Neuritis - Neu

Claw hand - CH

Foot drop - FD

Ulceration of Skin lesions - UL

Exacerbation - Exacer

Repeated Exacerbations - Rph Exacer

Bacteriological Index - BI

Epidermal Changes - Epi changes

Grenz zone - GZ

Infiltrate in dermis - Inf.D

Infiltrate in dermis & subatis - Inf D+S

Neutrophilic abscers - N.A

Panniculitis - Panni

Vasculitis - Vascu

REACTIONS IN LEPROSY CASE SHEET

Sex : Age : : Name

Occupation :

PRESENTING COMPLIANT

Anaesthetic / Hypoanaesthetic / Normoesthetic : 1. Skin Lesions

Duration Site

a)

b)

c)

2. Numbness

Duration Site

a)

b)

c)

3. Painful nodules

Duration Site

a)

b)

c)

4. Ulcers

Duration Site

Hands / feet

Other Sites

5. Weakness / Paralysis

Duration Site

a) Upper Limb

b) Lower Limb

c) Others

6. Deformity

Duration Site

a) Hands
b) Feet
c) Others

II.**H/O PRESENTING ILLNESS**

Onset & Duration:

Progress

Initial -

Late -

Y / N H/O Fever
Y / N H/O Swollen feet / hands
Y / N H/O Ulceration of the lesions / elsewhere
Y / N H/O Nasal stuffiness
Y / N H/O Epistaxis

Concurrent infections / illnesses

Y / N URI / LRI
Y / N UTI
Y / N Pain Abd
Y / N AGE
Y / N H / O Surgery
Y / N Emotional / Physical Stress

CONTACT HISTORY III

Present / Absent

TREATMENT HISTORY IV

Treatment started on:

Regime followed :

Other drugs given

Regular / Defaulter / Dropout

G / E

Ill / Mod / Well : Built

Ill / Mod / Well : Nairishment

Present / Absent : Anemia

Present / Absent : Jaundice

Present / Absent : Fever

Present / Absent : Clubbing

Present / Absent : Pedal edema

Present / Absent : Gen : Lymphadeno pathy

Present / Absent : Regional

: Site

: Joint Swelling

Hepatosplenomegaly :

: Orchitis

D / E

1 . Skin Lesions :

A)Site

B)Size

C) Shape

D) Symmetry

E) Number

Macule / Patch / Papule / Plaque / nodule / infiltration/ Ichthyosis F)Type of Lesion :

Face

: Ant Trunk
Post

Gluteal region :

: Arm Upper limbs
Forearm
Hands

: Thigh Lower Limbs
Legs
Feet

Any specific area / points deserving mention :

HP/Erythematous / Normopigmented/copper coloured /scar G) Colour of the Lesion :

: Face

Ant : Trunk
Post

Gluteal region :

Arm : UL
Forearm
Hands

Thigh : LL
Leg
Feet

Normal / Dry & Wrinkled / Succulent/ Scarred / Scaly h) Surface of Lesion :

: Face

Ant : Trunk
Post

Gluteal region

Arm : UL
Forearm
Hands

Thigh : LL
Leg
Foot

Tm-T-P- Present / Diminished / Absent i) Sensation of lesion :

: Face

Ant : Trunk

Post

Gluteal region

Arm
Ra : UL
Hands

Thighs
Legs : LL
Foot

PERIPHERAL NERVES :

SP PTN SUR LPN MED RAD RCN UN ST SO GA

L R L R L R L R L R L R L R L R L R L R L R

Thickening											
Tenderness											

Any feeding nerves:

Thickening:

Tenderness:

SENSATION OF EXTREMITIES:

Present / Diminished / Absent L a. Corneal sensation

Present / Diminished / Absent R

Present / Diminished / Absent L b. Face

Present / Diminished / Absent R

Present / Diminished / Absent L c. Palms

Present / Diminished / Absent R

Present / Diminished / Absent L d. Soles

Present / Diminished / Absent R

MOTOR ASSESSMENT

a. Face

	LID LAG	WRINKLE FOREHEAD	BLOW CHEEKS	SMILE	NASOLABIAL FOLD	EPIPHORA
	UPPER/ LOWER/ NIL	PRESENT/ ABSENT	ABLE/ UNABLE	DEVIATION ANGLE OF LIP PRESENT/ ABSENT	PRESENT/ ABSENT	PRESENT/ ABSENT
	UPPER/ LOWER/ NIL	PRESENT/ ABSENT	ABLE/ UNABLE	DEVIATION ANGLE OF LIP PRESENT/ ABSENT	PRESENT/ ABSENT	PRESENT/ ABSENT

b. Hands

	AB Di Min	DOR INT	PAL INT	FCU	Add Poll	LUMBRICALS	Opp Poll	Abd Poll	EXT WRIST

										I	M	R	L			

c. Feet

	TIBIALIS ANTERIOR	EXTENSORS OF DIGITS				EXTENSOR HALLUCIS LONGUS
		2	3	4	5	

DEFORMITIES

a. Face: Lagophthalmos Right/ Left

Right/ Left Facial

b. Hands: Ulnar claw Right/ Left

Right/ Left Ulnar median claw
Right/ Left Wrist drop
Right/ Left Ape thumb
Right/ Left Wasting thenar
Right/ Left Wasting hypothenar
Right/ Left Wasting lumbricals
Right/ Left Deviations fingers / toes
Right/ Left Resorption fingertips
Right/ Left Resorption toe tips
Right/ Left Swan neck
Right/ Left Hooding

c. Feet: Foot drop Right/ Left
Right/ Left Claw toes
Right/ Left Toe drop

d. Lepromatous leprosy:

Right/ Left Ear lobe thickening

e. Glove and stocking anaesthesia:

Present/ Absent Right upper limb
Present/ Absent Left upper limb
Present/ Absent Right lower limb
Present/ Absent Left lower limb
Present/ Absent Depression of nose
Present/ Absent Loss of incisors
Present/ Absent Hoarseness of voice
Present/ Absent Gynaecomastia / -thelia
Present/ Absent Infiltration of face

ULCERS
Present/ Absent FEET

Present/ Absent HANDS

INVESTIGATIONS

TC BLOOD

DC

ESR

HB

Bl. SUGAR

Bl. UREA

S. CREATININE

LIVER FUNCTION TEST

S. T. PROTEIN

S. BILIRUBIN

SGOT

SGPT

SAP

URINE ROUTINE

MOTION ROUTINE

SMEAR FOR MP/ MF

VDRL

HIV Ab

X-RAY CHEST PA VIEW

SPLIT SKIN SMEARS

BIOPSY

DIAGNOSIS:

REACTION GRADING:

FOLLOW UP:

DATE	CLINICAL PROGRESS	TREATMENT